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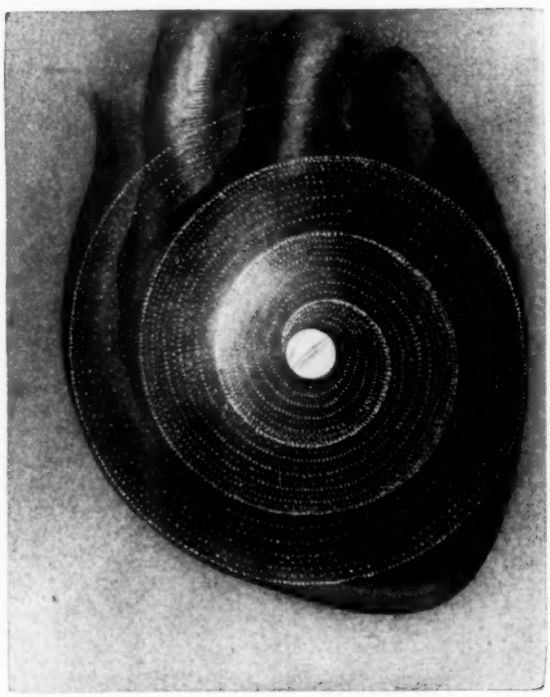

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VOLUME 217 NOVEMBER 18, 1937 NUMBER 21

MASSACHUSETTS MEDICAL SOCIETY

Section of Medicine

Presiding: Dr. Laurence D. Chapin, Springfield, chairman; Dr. George D. Henderson, Holyoke, secretary.

THE CHAIRMAN: Since Dr. Henderson and I were honored a year ago at the meeting in Springfield we have been working on the program for this afternoon. We thought it would be wise to have a symposium on treatment, and after much thought we decided to have one paper on fever therapy, one on the treatment of anemia, one on peripheral vascular disease, and one on some phase of psychotherapy.

Our first paper this afternoon is by Dr. Harry C. Solomon and Dr. Israel Kopp, and their subject is "Fever Therapy."

FEVER THERAPY

HARRY C. SOLOMON, M.D.,* AND ISRAEL KOPP, M.D.†

BOSTON

THE malarial treatment of general paresis as introduced by Wagner von Jauregg in 1917 gave an enormous impetus to the consideration of fever as a therapeutic agent. Of course fever therapy in one form or another had been used for a number of years in a variety of conditions. The use of typhoid vaccine fever was especially familiar in acute arthritis. Following the introduction of malaria, this method and other fever-evoking devices were tried in many conditions such as dementia praecox, multiple sclerosis, encephalitis, the various arthritides and many others. Not only were a variety of disease conditions experimentally treated, but interest turned to a development of methods of producing fever artificially by the use of various infections such as relapsing fever and rat-bite fever, chemicals such as sulfur in oil, and vaccines, but more especially to mechanical methods.

At the present time several mechanical methods of heat-production are taking an important place in fever therapy. A brief description of some of these methods may be in place. It can be stated at the outset that when the body's physiologic method of keeping the temperature from rising, namely evaporation of sweat from the body surface, is inhibited, fever will result. Taking advantage of this, several methods have been devised. The simplest is the hot bath. Under these circumstances the patient is put in a hot environment of 100 per cent humidity, with no possibility of evaporation taking place from a great portion of the body surface. This is a very effective method, but it is hard on the patient and too likely to lead to collapse. Simpson and his co-workers[1] developed an air-conditioning unit known as the Kettering hypertherm, in which the patient is surrounded by circulating air highly saturated with water. There are several machines on the market having a similar basis of fever production. Using a principle somewhat the same, but requiring a different mechanism, is the method of throwing vaporized hot water on the patient, known as the hydro-eneciator.[2] The so-called electric blanket is a device which consists essentially of an enlarged electric heating pad which surrounds the patient, heats the environmental air, and prevents evaporation from the body surface. Electric waves thrown on the body raise the temperature by a different mechanism. Several varieties of electric heating are available, including the short-wave radio field and diathermy, and attention is now being given to the inductotherm, in which the patient is put into an electromagnetic field. Radiant and luminous heat as developed by an ordinary tungsten light or a carbon-heating filament produces both environmental heat and some absorption of the heat through the skin. A combination of two or more of these methods is likewise available and often used.

From the Boston Psychopathic Hospital.

Presented at the annual meeting of the Massachusetts Medical Society, Boston, June 1, 1937.

*Associate professor of psychiatry, Harvard Medical School.

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GONORRHEA

The two conditions in which fever therapy seems the most rational and in which the best results have been obtained, and in which we have the largest amount of experience, are gonorrhea and syphilis. In both, one deals with organisms which are quite readily destroyed by a relatively small increase in temperature above normal. Most is known about the "thermal death" time of the gonococcus owing to the work of Carpenter and Boak.[3] They made determinations of the length of time required to kill various strains of gonococci at a temperature of 106.7°F. They studied as many as two hundred and fifty strains of the organism, and found that the time required to sterilize such

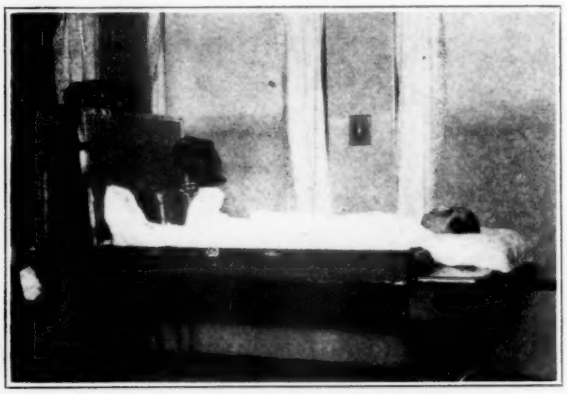

Fig. 1. *Kettering hypertherm. Patient ready to be placed in cabinet.*

cultures varied from six to thirty-four hours. On the basis of this information, Warren[4] treated 100 consecutive cases of acute gonorrheal infection by subjecting the patient to a temperature of 106.7°F. for the number of hours that it took to kill a culture from the given case at this temperature level. He reports that 87 of the cases were cured bacteriologically and clinically at the end of one treatment; in 8 cases the cultures were positive but the viable organisms disappeared within from three days to six weeks following the fever treatment, either spontaneously or while the patient was under local chemical treatment. Four additional cases in women were not cured after the first treatment; cultures taken after unsuccessful treatment were found to be more heat-resistant than were those taken originally. In 1 case death occurred.

In another series of 163 cases where fever was given for a period less than that required to kill the cultures, a single treatment of from five to fifteen hours resulted in cures of from 20 to 60 per cent.[4] The work of Warren, Carpenter and Boak seems to establish fairly well that the gonococcus dies when the body temperature is raised a sufficient degree for a sufficient period of time, and also that it is possible to give patients temperatures that are lethal for the gonococcus. Warren has treated patients with a higher temperature for a longer time than anyone else. The majority of those using the febrile method of treatment have not been willing to subject patients to such a strenuous therapy, but have adopted a more conservative procedure. Even under these circumstances the treatment of gonorrheal urethritis has shown quite remarkable results. A compilation of 1045 cases, in which patients were both male and female, and which included those with complications, treated by fever, the time and height of which varied considerably with the different therapists, indicates that 87 per cent were cured, 5.5 per cent were improved, and but 7 per cent were failures; 1 death was reported. Several different technics have been used; these we shall not discuss here further than to say that Bierman and Horowitz,[5] in treating gonorrhea in the female, especially with pelvic involvement, have not only used general fever but in addition have given local diathermy through a vaginal electrode, raising the local temperature to from 109° to 110°F. Several modifications of local fever have been introduced.

The results achieved in gonorrheal arthritis are extremely dramatic. Warren and his associates[6] treated it by the system which they used in urethritis, namely finding the "thermal death" time for the organism and treating the patient accordingly. Others, using empirical methods with the temperature approximately 106°F. for from five to seven hours on each treatment day, also obtained striking results.[7, 8, 9] In 120 cases reported by five therapists, cures were reported in 72 patients, while 35 had marked relief, and only 2 had no relief; in 11 cases no statement was made as to result. In our experience we have had 5 acute cases. In each the patient showed improvement as soon as five hours of fever treatment were over, the improvement was maintained, and with further treatment complete relief was obtained.

SYPHILIS

General Paresis. In discussing fever treatment for syphilitic infections, one may well begin with general paresis because historically this was the first variety of lues to receive intensive study in this type of treatment. It is hardly necessary to review the results of fever therapy in general paresis; practically all investigations have shown that approximately 70 or 80 per cent of the cases treated have been arrested. The majority of patients to whom fever has been given have had it by means of malaria; a variety of other methods have also been used. As regards results, there is a marked

divergence in the percentages given by various investigators, whatever the method used. In comparing small series of cases, therefore, little value should be placed upon conclusions drawn as to the exact proportion of favorable, moderately favorable and unfavorable results.

Interest at the present time is centered on whether mechanically produced fever is more effective than that given through malaria. Consideration of this question is largely theoretical. First, is fever alone the potent therapeutic essential, or have immunity responses, stimulation of the reticuloendothelial system or other effects the greatest meaning? Certainly with mechanically produced fever high temperatures are sustained longer than is usual with malaria treatment. A few attempts have been made to compare results. Thus, Barnacle, Ebaugh and Ewalt[10] compared two series of 30 cases each. The patients treated by artificial or mechanical fever received an average of 44.5 hours of fever at 105-106°F., and at the height of fever were given 2 gm. of tryparsamide intravenously, and later weekly injections of tryparsamide. Those receiving malaria were inoculated with a tertian strain. There were on the average ten elevations of temperature. Following malaria they were given six doses of neoarsphenamine at semiweekly intervals, and then weekly injections of tryparsamide. The results were as follows:

Result	Artificial Fever		Malaria	
	No.	*%*	*No.*	*%*
Complete arrest	12	40	7	23
Improved	9	30	12	40
Unimproved	8	27	7	23
Died during treatment	0		1	3
Died subsequent to treatment	1	3	3	10

The findings as regards the spinal fluid were as follows:

Result	Artificial Fever		Malaria	
	No.	*%*	*No.*	*%*
Completely negative	4	13	0	—
Greatly improved	3	10	4	13
Moderately improved	3	10	8	27
Unmodified	17	57	10	33
Unknown	3	10	8	27

The results indicate the superiority of fever induced by artificial means, but in so small a series they cannot be regarded as conclusive. In the spinal fluid findings the results do not differ very greatly. One should bear in mind that the longest period of observation in this series was approximately fifteen months, and that changes in the spinal fluid are as a rule delayed over a period of several years. The significant finding of these authors is that with mechanical fever they did get four completely negative fluids in a relatively short period, which is very rare in malaria-treated cases. On the other hand, if one considers improvement of the spinal fluid the malaria series gives more favorable results.

Neymann[11] made a compilation of cases from the literature. He quotes Kraepelin as having analyzed 3000 cases treated by malaria, with improvement in 43 per cent, whereas in cases of mechanically induced fever collected by Neymann, improvement was found in 63 per cent. Kuhns[12] made a comprehensive study of his own cases treated from 1927 through 1932 by several means, as follows:

Form of Therapy	No. of Patients	Results: Improved	Unimproved	Worse
		%	%	%
Typhoid	100	52	28	20
Sulfur in oil	100	58	21	21
Malaria	100	66	20	14
Diathermy	100	72	11	17
Electric blanket	100	78	15	7

In 1934 he treated 247 patients by several methods with the following results:

Form of Therapy	No. of Patients	Results: Improved	Unimproved	Relapsed	Died
		%	%	%	%
Malaria	96	68	16	4	12
Electric blanket	40	60	28	12	0
Sulfur in oil	60	35	55	0	10
Typhoid	27	74	26	0	0
Combined forms	24	46	42	4	8

Another consideration when comparing methods of treatment is the mortality rate. Here again the

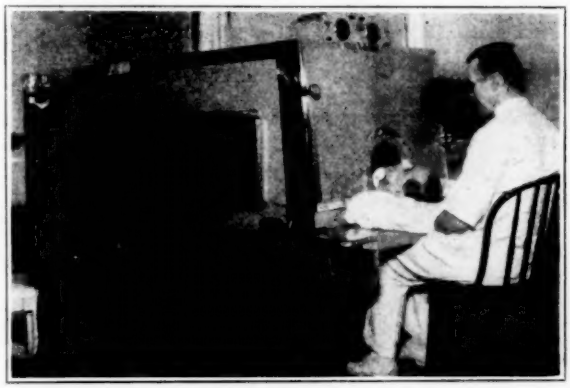

Fig. 2. *Kettering hypertherm. Patient in cabinet.*

results are so divergent that it is utterly impossible to reach any adequate conclusions. Particularly in paresis, patients who are extremely poor risks are often justifiably treated, and if these are included in the calculation the mortality rate will be much higher than where a selection of cases is made. Furthermore, a considerable number of patients are going to have a relatively short life whatever the type of treatment. Some investigators consider that a patient who dies within from six months to a year after treatment is to be placed in the death column, while others are willing to consider in this group only those patients who die during or immediately after malaria as an obvious result of it. Consequently we find some reports of a mortality rate above 20 per cent, while at the Mayo Clinic, according to Woltman,[13] in a series

of 800 cases the rate was less than .5 per cent. In our own experience the death rate when figured rather liberally is approximately 3 per cent.

Which of the many methods of evoking fever is the most satisfactory in general paresis is a question we are unable to answer. A study of the literature has not convinced us one way or the other, and our own experience of more than six years with mechanically produced fever and twelve years with malaria-produced fever has failed to bring us a positive conviction. We are still pleased with malaria as a therapeutic measure. It is certainly cheaper and simpler, and when properly utilized is by no means more dangerous than the others.

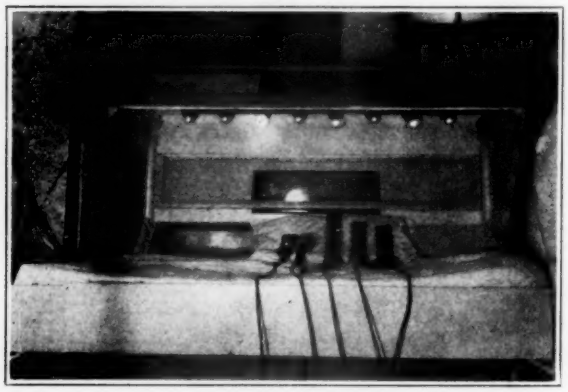

Fig. 3. *Cabinet for combined diathermy and radiant heat.*

Tabes Dorsalis. If there is difficulty in evaluating the results of treatment in general paresis, this is many times multiplied in dealing with tabes dorsalis. It is very difficult to present briefly an adequate analysis. The consensus over a period of years has been that malaria is not so effective in the treatment of tabes dorsalis as it is in general paresis. By this is really meant that in a good many cases pains or gastric crises persist after the serology has become negative, or that new symptoms, such as bladder disturbances, occur during malaria, or that despite what appears to be an excellent immediate result there later appear Charcot arthropathies; finally, so many cases of tabes do extremely well under chemotherapy that there is less reason for fever therapy except in the rather advanced cases or those occurring in individuals in later life. A number of investigators, among them Bennett,[13] Mehrtens and Pouppirt,[14] and Simpson,[15] report considerable to marked relief of lancinating pains through the use of mechanically produced fever. The literature is likewise replete with instances of similar relief by malaria. Our own experience has been quite similar. Gastric crisis cases, on the other hand, do not show such uniformly good results. The cases reported indicate that about half the patients are relieved. Our results have been universally unsuccessful, but it may be said in justification that we have treated patients who after a long period of chemotherapy had become serologically improved but had not had corresponding relief of their gastric crises. A bout of fever seems to be capable of stopping a particular crisis, but not necessarily of preventing recurrences.

Optic Atrophy. It is generally believed that fever rarely produces any improvement in the vision of patients with primary luetic optic atrophy.[16, 17] While there have been but few favorable reports concerning improvement of vision,[18, 19] notably that of Breutsch, there is more to be said about the arrest of the progress of atrophy, although there is by no means uniformity of opinion. While the literature has not contained very many reports, most authors with experience seem to think that a good many cases are apparently slowed up and that fever is worth trying; but there is hardly any optimism or conviction that the majority of cases can be permanently arrested.

Early Lues. Weichbrodt and Jahnel[20] in 1919 showed that rabbits with experimental chancres could be sterilized by repeated baking at a temperature consistent with the life of the animal. In 1926 Schamberg and Rule[21] again studied the "thermal death" point of a *Spirocheta pallida* in experimental rabbit syphilis. The technic was to immerse the rabbit in a hot bath at a temperature of 113°F. for from fifteen to twenty minutes daily for twelve days. Their studies convinced them that fever so produced was effective in preventing the development of the disease in inoculated animals, and of clearing up the lesions once produced. As a result of these experiments, Schamberg and Tseng[22] turned to the treatment of human patients who had early syphilis, using the hot-bath method to produce fever. They found that although this method gave some results in weakening the serologic tests and brought clinical improvement, it did not suffice to cure the disease.

Within the last two or three years more attention has been given to the place of fever therapy for the treatment of early syphilis. In 1935 Simpson[15] reported on the treatment of 6 cases of primary and secondary syphilis by fever alone. In 2 of these cases, relapses occurred. He therefore added chemotherapy. In 1936 Neymann, Lawless and Osborne[23] treated 7 cases of primary and secondary syphilis, and got results which were very similar to those of Schamberg at an earlier date; that is, there was partial arrest but relapses occurred, and they concluded that hyperpyrexia alone was not a satisfactory treatment. Epstein

and Cohen,[24] also in 1935, reported on the treatment of 33 cases with practically identical conclusions. In 1936 Neymann, Lawless and Osborne[23] reported on 7 additional cases of primary and secondary syphilis which were treated by a combination of fever and chemicals consisting of neoarsphenamine and bismuth. These patients received treatment for an average of forty-two days without any evidence of serologic or clinical relapses over a period of from five to eight months of observation. In 1935 Simpson[15] reported on 26 cases treated with a combination of fever and chemotherapy, and in 1937 reported[25] further on a series of 34 patients with early syphilis treated by this combination. All conclude that artificial fever fortifies and intensifies the curative action of the chemicals; that the time required for the adequate treatment of early syphilis can be greatly reduced; and that the combination of fever and chemicals may allow for smaller doses of drugs.

Interstitial Keratitis. The literature indicates that interstitial keratitis in its acute inflammatory state is greatly helped by fever therapy. Culler and Simpson[16] report 11 cases treated with fever and chemotherapy, and conclude that recovery is greatly hastened, recurrences are fewer, and the tendency to spread to the other eye is reduced. Doub[26] reports on 2 cases in which the inflammation cleared. McGavic,[27] in a series of 7 cases, is quite impressed with the results. We have treated 9 cases, and are likewise impressed with the fact that the inflammation and photophobia were quickly improved, even though we used no associated chemotherapy.

Results have also been reported in a few cases of uveitis, acute iritis, optic neuritis and active choroiditis, with encouraging results.[16, 27]

OTHER DISEASES TREATED BY FEVER

The list of other conditions that have been treated by fever, often experimentally, and at times without clearly defined reasons for so doing, is very great. In fact Krusen,[28] in an article in 1936, lists fifty disease conditions that have been subjected to heat therapy.

Arthritides. Interest has been especially marked in the arthritides; most study has been devoted to the effects of fever on *infectious, atrophic or rheumatoid arthritis.* The results have certainly not been outstandingly successful. They do not in any way compare with those achieved in gonorrheal arthritis. As to whether fever therapy actually produces noteworthy improvement, there is no complete agreement. A survey of 265 cases reported by several workers is interpreted by them as showing 8 per cent of the patients cured, completely relieved, or freed of symptoms. Marked or moderate relief was obtained in 53 per cent, whereas 33 per cent received little relief or were unimproved, and 6 per cent were worse. The investigators further report that of the patients who apparently did well nearly all relapsed,[7, 29] so that a careful consideration of the results led them to expect very little benefit from this type of treatment. Thus, Short and Bauer[29] conclude from their 25 cases that the severity of this type of treatment and the paucity of its results do not justify its continuation. Cecil[30] finds the results disappointing, and Stecher[31] states that of his series none were cured. On the other hand, Kohn and War-

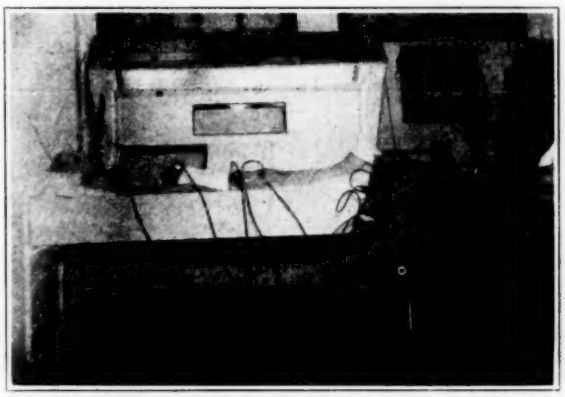

Fig. 4. *Combined diathermy and radiant heat. Electrodes in place, and patient ready for cabinet to be closed.*

ren[32] are much more pleased, reporting more than 80 per cent of their 43 cases as either moderately or markedly improved; where relapses occurred, they felt that further improvement would result from additional treatment.

The literature discloses 74 cases of *hypertrophic arthritis* treated with fever. Complete relief of symptoms was obtained in 4 per cent, 53 per cent were improved, and 43 per cent were unimproved. Simpson,[33] in summing up the results of treatment in hypertrophic arthritis, says that it is definitely disappointing.

There occur reports of various *unclassified types of arthritis* treated. Thus, under the heading of chronic arthritis Simpson[33] reports 20 cases, and Bishop, Horton and Warren[34] report 15 cases, stating that some relief was obtained. Auclair[35] reports 80 cases consisting of monoarthritis, ankylosed arthritis, hip arthritis, vertebral arthritis, lumbago, sciatica and neuritis treated by fever produced by short-wave therapy, with only 7 failures; but one cannot tell which type of case was relieved. Tenney (quoted by Hench et al.[7]) reports 6 cases of neuritis without specifying the type, of which 5 became symptom-free; 8 cases of myositis, of which 2 became symptom-free and 2 improved; and 4 cases of bursitis, of which 2 became symptom-free and 2 improved. Stecher[31] reports 6 cases

of arthritis of the spine, with relief of pain but no increase of motion.

Acute Rheumatic Fever. We have found but one report on fever therapy of acute rheumatic fever. This is a summary of 15 cases by Simmons and Dunn.[36] They list 13 cases completely relieved of pain and swelling, 2 relapses, and 1 case which developed chorea twenty months after the fever.

Sydenham's Chorea. The results reported in the treatment of Sydenham's chorea have been on the whole enthusiastic. One hundred and sixty-seven cases have been reported by five different groups of observers. As given they are not readily translated into percentages. Barnacle, Ewalt and Ebaugh[37] treated 45 cases with what they consid-

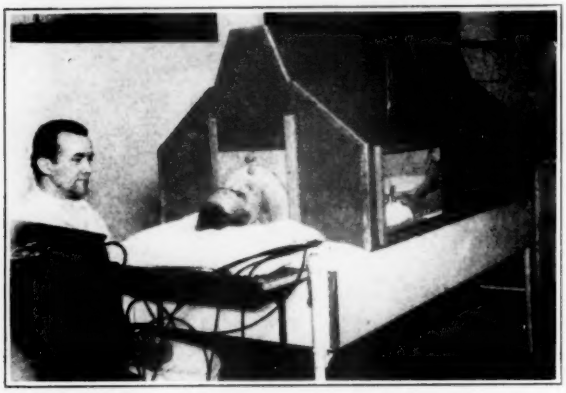

Fig. 5. *Combined diathermy and radiant heat. Patient in cabinet.*

ered excellent results in most, but with 3 recurrences. Sutton and Dodge[38] treated 50 cases and considered the length of the disease definitely shortened. Schnabel and Fetter[39] treated 10 cases; of those 8 treated with a temperature of 105 to 106°F. results were excellent and 2 treated with 103 to 104°F. showed striking improvement. Neymann, Blatt and Osborne[40] treated 56 cases, of which 50 were cured and 6 showed recurrences. Metz[41] treated 6 cases, and reported that all movement ceased from two to four weeks after treatment. We have treated but 1 case of chorea, with complete cessation of movement after one session at a temperature above 105°F. for five hours. Each of the investigators has found that complicating carditis is not a contraindication to the use of fever therapy, but on the contrary, reports improvement in this condition.

Asthma. There are four reports on the fever treatment of chronic asthma. In each instance the cases submitted to fever therapy were said to have been chronic intractable asthma in which all the usual types of treatment had been applied but without success. Feinberg, Osborne and Afremow[42] reported in 1931 that they had treated 37 patients with "encouraging results." Phillips and Shikany[43] reported on 50 patients, treated with clinical relief in 40, no relief in 7, and 3 worse after treatment. Sheldon[44] treated 14 asthmatics, of whom he considered 6 as markedly improved, 4 slightly to moderately improved, and 4 unrelieved. Metz[45] had 8 patients under treatment, of whom 3 obtained complete relief, 4 were slightly improved, and 1 showed little or no improvement. None of the authors felt that the results were long-lasting, as relapses occurred after a period of several months in most cases that had received apparent benefit. However, one gets the impression that they felt that the relief was often sufficient to justify the treatment, as some patients who were completely incapacitated were able to return to some sort of satisfactory activity. It may be added that Feinberg and his co-workers[42] state that they applied fever therapy because asthmatics were usually relieved somewhat of their attacks after having had a febrile disease from whatever cause, provided it was outside the respiratory tract. Phillips and Shikany[43] argue that asthma represents in its final analysis a partial sympathetic collapse, and that fever should be useful because it is a good method of stimulating the sympathetic nervous system.

Multiple Sclerosis. Fever treatment of multiple sclerosis has been given a good deal of publicity in lay magazines, as a result of which a great many patients have asked for and obtained this type of treatment. Multiple sclerosis is a disease in which it is particularly difficult to make an evaluation of symptomatic improvement, because there is a strong tendency toward natural remissions followed by recurrences. Furthermore, most patients are euphoric and optimistic, and are likely to report improvement under therapy. There are a large number of reports of the treatment of this disease, but it is especially difficult to evaluate satisfactorily the effect of treatment. A report of the largest group in the literature (144 cases) was published by Weiss[46] in 1935. He states that 65 per cent were definitely improved, the remaining 35 being unchanged. The average remission period was fifteen months. The most frequent improvement was that in motor power and spasticity (75 per cent); ankle clonus disappeared in 42 per cent; ataxia improved in 35 per cent; sphincter disturbances were benefited in 25 per cent; Babinski signs disappeared in 18 per cent; temporal pallor cleared in 10 per cent; while nystagmus showed no change. This report is certainly the most encouraging and enthusiastic that has so far appeared. Neymann and Osborne[47] reported in 1934 on 25

patients observed from a few weeks to 8 months. Of these, 11 were much improved, 10 moderately improved, 1 relapsed, 2 died, and 1 was unaccounted for. Perkins[48] reported in 1933 on the treatment of 15 cases without giving actual details of each case, but thought that there was real improvement in both gait and sensation. In 1937 Russell[49] reported on 15 cases, of which he considered 6 as improved, 4 as unchanged, and 5 as worse. We have treated 15 cases without being much impressed by the results. Many of the patients have reported that they feel better, but in most of them objective evidence of marked improvement is lacking. One patient who made a very good improvement had had two or three previous paralytic attacks, from which she had recovered spontaneously. Two patients with spastic paraplegia reported themselves as distinctly worse following the treatment. On the whole, there is no objective evidence of improvement in these 15 cases that can be definitely accredited to fever, and there is an equal chance of the patient's becoming worse. Possibly in the very acute cases some value may accrue from treatment.

Tuberculosis. Studies have been made on the effect of fever therapy on tuberculosis. While it is recognized that the temperature to which the body can be safely subjected is well below the death point of the tubercle bacillus, it has been argued that possibly the subjection of the organism to relatively high temperatures might inhibit its growth and afford the host a better opportunity to combat its activities. Major, Doub and Hartman[50] treated a series of dogs that had been experimentally inoculated intratracheally and intravenously. Following treatment they thought that there was temporary improvement in the dogs, which showed increased activity, better appetite and a lower temperature. They also found that the lives of the treated animals were prolonged as compared with a control group. Doan and Bierbaum[51] in experimental work with rabbits were sure that the fever as they used it was harmful. Duncan and Mariette[52] treated 34 cases of pulmonary tuberculosis by fever, induced either by diathermy or by the Kettering method. They report that 21 per cent were moderately improved, 52 per cent slightly improved, 21 per cent showed no change, and 6 per cent were worse. However, they add that in no case was the cavity closed, the sputum did not become negative, and improvement was on the whole slight, and of theoretical rather than practical importance. They do not recommend fever treatment for pulmonary tuberculosis in human beings.

Subacute Bacterial Endocarditis. Schnabel[53] treated 2 cases of *Streptococcus viridans* endocarditis by hyperpyrexia. He reported that the patients stood the treatment well, they had an improved sense of well-being, and the temperatures became normal, but they both succumbed to the disease.

Faget[54] treated 1 patient to whom he gave three fevers at 107°F.; although extreme vasomotor collapse occurred in one treatment, the night sweats ceased, and the blood cultures became consistently negative; but the patient died a few months later of a cerebral embolus. Bierman in discussing this report told of a case in which marked multiple emboli were found after treatment, and Simmons reported a case treated with

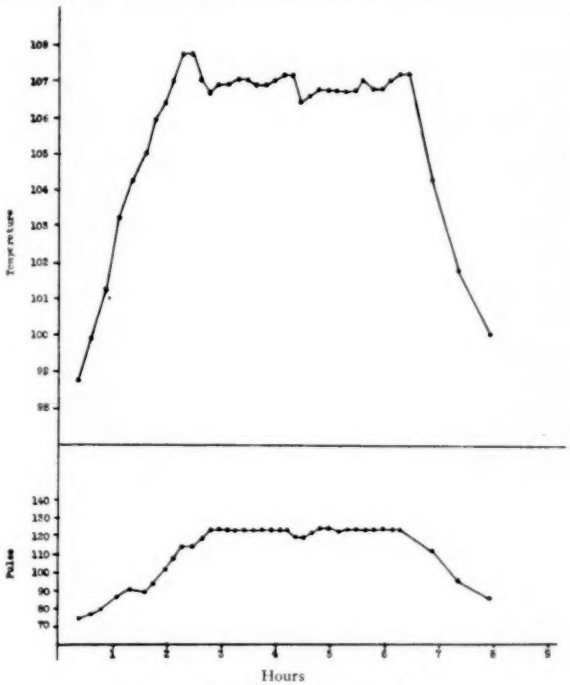

Chart 1. *Hypertherm hyperpyrexia.*

temporary relief but with death from cerebral embolism. Freund and Watts[55] treated 3 cases with quite high temperatures, using 107 or 108°F. for several hours and 108 or 109°F. for one hour. They used these high temperatures in the first place because they recognized that the *S. viridans* is rather heat resistant, but more especially because of a recovery seen by one of them in a *S. viridans* infection following a temperature of 108°F., resulting from an intravenous injection of glucose. The results as they saw them in their 3 cases were that the strength of the patient improved and there was less rise in the daily temperature over a period of months; the blood cultures remained positive, however, and the patients finally succumbed. It appears that as yet there is no evidence that fever therapy is a successful agent for treating subacute bacterial endocarditis.

Osteomyelitis. Doub[56] reports 4 cases of osteomyelitis treated by hyperpyrexia. In a case of os-

teomyelitis of the mandible which was previously resistant to other forms of treatment, marked relief was obtained and the lesion healed. In a second case of postoperative osteomyelitis of the bones of the face, which the author says is almost 100 per cent fatal, a perfect result was obtained by four or five fever treatments. Another case similar to the second, with a walled-off abscess, died after fever treatment. A fourth case, in which there were cystic lesions of several long bones and generalized septicemia and marked debility, did not improve and died of a septicemia.

Mycosis Fungoides. Klauder[57] reports on 2 cases of this disease treated by him, and reviews 5 cases from the literature. He states that there have been spontaneous improvements in this condition following acute febrile states. He found 5 reported cases that had been treated with malaria, with favorable results in 4. He states that although malaria treatment does not cure the lesions, it produces an effect which is important. Of his 2 cases, the first patient was a man, fifty-six years of age, whose lesions had started six years before fever was given. X-ray had given some relief for a time. Later it did not relieve the itching. Then typhoid vaccine was given intravenously in six doses, producing a temperature of from 102 to 103°F., but without relief. Finally he was given malaria and had ten paroxysms, with the temperature varying from 103 to 105.6°F. There was some immediate relief, and six months after the malaria the improvement was considerable. Two years later he was in good condition, although the lesions still persisted. At the end of twenty-nine months he relapsed, then was given fever by the Kettering hypertherm, and seemed to be improving once more. The other patient was a fifty-three-year-old male who was given twelve fever treatments of from four to five hours' duration at 104 to 105°F., with improvement. In the discussion of Klauder's results, O'Leary states that he himself treated 2 cases with malaria and 3 with the Kettering hypertherm, and noted slow progressive improvement. Corson treated 1 patient with fever produced by a hot-water spray, with considerable improvement. Lane treated 1 case with sulfur and typhoid hyperthermia without results, and the disease progressed to a fatal termination.

Tumors. It has been reported many times in the literature that apparent spontaneous improvements of malignant tumors have occurred following severe infections with fever. Furthermore, Coley serum usually produced high fever. So, as might be expected, attention has been once more turned to the effect of fever on tumors. Thus, Jares[58] has shown that rat carcinosarcoma is killed by a temperature of 41.5°C. sustained for thirteen hours or by a temperature of 42°C. for seven hours; that the cells of mouse tumors died after being exposed to 41.5°C. for fifteen hours or to 42°C. for eight hours, and that the rat tumor cells were killed in thirty hours at 42°C. He also found that in vivo a combination of fractional x-ray and fever therapy in rabbit epithelioma of the testis gave local cures approximately double those of either type of therapy separately. In attempting to apply these experimental findings of the combination effect of fever and x-ray therapy to malignant tumors, Warren[59] treated 31 cases of what he considered hopeless malignant disease. In summarizing his experience he states that in cases previously treated by x-ray and previously untreated cases, fever seemed to have a definite destructive effect on the tumor cells. The amount of destruction and its duration varied from case to case. No results approaching cure have been obtained by this procedure.

Brucellosis. Prickman and Popp[60] report on 3 cases of brucella infection treated by the Kettering hypertherm, each patient receiving three treatments. In each case improvement was considered as occurring, and from the standpoint of clinical observation cure resulted. They comment on the interesting fact that the organism in vitro is resistant to heat of 107°F. for twenty-four hours, and therefore assume that apparent improvement in the patient was not the result of sterilizing the infection.

Meningococcal Infections. Moensch[61] found that the meningococci reacted to heat in vitro much as do the gonococci. In her experiments she found that of a great many strains of meningococci all but one showed a reduction in growth when submitted to a temperature of from 40 to 42°C. for from five to seven hours. Five strains were destroyed or greatly reduced in five hours or less, seven strains showed moderate reduction in growth, two only slight reduction, and one was not affected in seven hours' exposure. Bennett, Person and Simmons[62] treated 2 cases of chronic meningococcus septicemia with meningitic recurrences and obtained cures in each. They therefore recommend fever as an adjuvant therapy in subacute or chronic cases that are not relieved by serum.

SUMMARY

A short review is given of the present status of fever therapy, including descriptions of various methods of induction, such as malaria, typhoid vaccine, diathermy, luminous-radiant heat and hot, humid environmental air. The clinical applications and results of treatment in a variety of disease conditions are discussed, and an analysis of

the literature is presented. A very brief recapitulation follows.

Excellent results are obtained in: (1) acute gonorrhea and in many gonorrheal complications including arthritis, epididymitis, orchitis, pelvic inflammation and ophthalmia; (2) neurosyphilis in most of its forms; (3) early syphilis when fever is combined with chemotherapy; (4) late syphilis with symptoms of inflammatory nature, namely iritis, interstitial keratitis and periostitis; and (5) Sydenham's chorea. There is division of opinion on the value of fever therapy in: (1) infectious or rheumatoid arthritis and other forms of arthritis; (2) chronic asthma; and (3) multiple sclerosis. No definite results but interesting experiences are reported in: (1) tuberculosis; (2) subacute bacterial endocarditis; and (3) malignant tumors.

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Discussion

THE CHAIRMAN: The discussion will be opened by Dr. John G. Gibson, 2nd.

DR. JOHN G. GIBSON, 2ND, Boston: A study of changes in water balance and blood electrolytes during fever therapy is now in progress at the Boston Psychopathic Hospital under the direction of Dr. Solomon. The results of this

study indicate that two main physiologic disturbances take place in the fever patient. The first is the great loss of water through evaporation of sweat; the second is the considerable loss of carbonic acid through hyperventilation in the effort to lower body temperature. The result of these changes is a lowering of the circulating blood volume and the development of alkalosis. It is therefore necessary to combat these changes by administration of water containing chlorides, and carbon dioxide. The success of any fever treatment depends in large measure upon the effectiveness of this replacement.

These changes may be considered as taking place during two periods of a bout of fever: during induction to the desired temperature level, and during prolongation at that level. The most drastic and sudden changes take place during the former period, when the body temperature rises in an hour and a half or two hours from a normal level to 105 or 106°F. We have studied these changes in patients treated with diathermy, diathermy in closed cabinets where hot moist air is circulated, and in cabinets heated by carbon filament lamps. Although patients vary somewhat in their reactions to high environmental temperatures, sweating during the period of induction is always profuse. The resulting loss of water, judged by ordinary clinical standards, is great. This loss represents a direct withdrawal of fluid from the blood stream via the sweat glands, and may proceed at such a rapid rate that the inflow of tissue fluids into the blood stream cannot keep pace with it. As a result, plasma volume may become greatly reduced by the time temperature has reached the desired level.

The amount of water lost during induction varies with the type of apparatus employed. Types that permit evaporation of sweat appear to be the most dehydrating. Cabinets in which the patient lies in a limited space through which the air does not circulate and in which the differential temperature between patient and environmental atmosphere is least appear to be the least dehydrating.

The amount of water loss during induction also bears a relation to the quantity of fluids, and the method by which they are given. The behavior of patients varies. Judging the degree of water loss by the percentage reduction in plasma volume from prefebrile levels, we have encountered patients who had a less reduction on fairly restricted intake than others who were liberally supplied by mouth. It is safe to say, however, that reductions in plasma volume ranging from 10 to 20 per cent may be expected during fever induction when fluids are given by mouth. When fluids are given intravenously, volume can be maintained at prefebrile levels.

One of the results of this sweating is a severe loss of chlorides. And since the body temperature is artificially maintained at a high level, the auxiliary cooling mechanism, namely hyperventilation, is called into play. This causes a loss of carbon dioxide. In addition, the loss of fluid from the blood stream brings about a concentration of all the blood electrolytes. As a result, a degree of alkalosis develops which may be severe, and which if unchecked may bring the patient into grave danger by the time the temperature peak is reached. We have measured changes in the pH of the blood serum up to 7.6 during induction of fever in patients who received large amounts of fluids.

On account of these changes, the patient enters the period of fever prolongation in varying degrees of dehydration and alkalosis. Maintenance at the desired level from then on depends on the effectiveness of replacement therapy. While the rate of fluid loss decreases after the temperature peak has been reached, it continues at a relatively high level, and in general bears an inverse relation to the amount of fluid given. Our studies indicate that the minimum fluid requirement, when given by mouth, is between 300 and 600 cc. an hour, depending on the type of apparatus used. The danger of over-hydration from orally administered fluids is little indeed.

There is evidence that the absorption of fluid from the intestinal tract is delayed at high temperatures. One of our patients was subjected to two bouts of fever of comparable degree and duration. During one treatment fluids were given by stomach tube at the rate of 670 cc. per hour; the plasma volume underwent a reduction of 11 per cent. In the other treatment, fluids were given intravenously at the same rate, and the plasma volume was maintained and increased slightly above prefebrile levels. In both instances there was an equal gain in weight at the end of treatment. In the former instance the fluid lay in the intestinal tract unabsorbed during the time it was most needed for replenishment of volume and tissue fluids.

As a result of continued uncompensated water loss, the circulating volume tends to fall steadily during prolongation of fever, depending upon the hours of prolongation and the rate of fluid intake. We have measured losses, based on plasma volume, loss, and weight changes up to 700 cc. per hour and over. This reduction could perhaps be well borne by a person at a normal temperature, but it becomes a serious matter when the changes in circulatory dynamics are added. During fever, the systolic pressure rises, at times to 150 mm. of mercury or more, the diastolic pressure falls to 0 mm. of mercury; the venous pressure rises, probably owing to transmission of arterial pressures through the widely dilated peripheral capillary bed; the pulse rate rises to 160 or more and the blood velocity is greatly accelerated, changing from a normal value of 20 seconds to 6 seconds at the height of fever. Cardiac output is increased. Tissue metabolism may be increased from 50 to 60 per cent over normal. In the face of the burden so placed upon the oxygen-carrying mechanism of the body, a diminished total volume cannot but act as a source of cardiac and respiratory embarrassment. The result is anoxemia. This leads to further capillary damage, which permits of a further reduction in plasma volume through extravasation, and thus a vicious cycle is established.

Accompanying this change is the mounting alkalosis. The loss of carbon dioxide and chlorides continues. The increased production of weak organic acids as by-products of increased tissue metabolism tends to fix more base. Relative anuria develops in the face of dehydration, preventing the excretion of excess base via the kidneys. The total base rises, and the concentration of bases is further increased by loss of water from the blood stream. The prevention of these changes is again the effectiveness of fluid and electrolyte replacement.

In summary, the patient undergoing a fever treatment, in addition to the thermal changes to which he is subjected, experiences a period of varying degrees of dehydration and alkalosis. Failure to take these threatened dangers into consideration will result in profound peripheral vascular collapse and damage to the central nervous system. Careful attention to fluid and electrolyte replacement will ensure the safety of the patient.

We feel that not enough information is available to the fever therapist on the nature and degree of the changes he may expect to take place in his patients. We also feel that sufficient investigation, from the point of view of these changes, of various types of apparatus now being offered to the medical profession has not been made. More attention should be given to this aspect of fever therapy, in addition to the evaluation of clinical results.

THE CHAIRMAN: The next paper is by Dr. William Dameshek, and is entitled "Physiologic Principles in the Treatment of Anemia."

PHYSIOLOGIC PRINCIPLES IN THE TREATMENT OF ANEMIA

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BECAUSE anemia is so obviously abnormal, it has always aroused medical curiosity. For many years the distinction between the lay term "pallor" and the medical term "anemia" meant very little so far as exact knowledge was concerned. Although distinctions were made between so-called primary and secondary types, very little progress was made in understanding the physiologic processes concerned in the development of anemia until about twenty years ago. The accelerated interest in the study of anemia following the remarkable success of liver therapy in pernicious anemia has led to many fundamental discoveries, among which may be listed the conception that the gastrointestinal tract and pernicious anemia are closely interrelated, the development of knowledge regarding the iron-deficiency state, and the important realization that anemia is frequently a manifestation of a generalized deficiency state.

Anemia may be defined as that portion of an abnormal bodily state which is characterized by a reduction either in the hemoglobin or in the red blood-cell content. Undue attention has often been paid to anemia as such, to the exclusion of the underlying abnormalities which have brought it about. Except possibly after hemorrhage, anemia is never an isolated phenomenon but is always an integral part of a more widespread disturbance. It is probably best, therefore, to consider anemia as a symptom, comparable in nature to dyspnea and cyanosis. According to this conception all anemia may thus be considered *secondary* to some cause, whether or not this cause is readily discernible. If this premise is correct, there can be no primary anemia, and the designation "secondary" is meaningless, so that other terms must be used. Before discussing these, however, we shall review the processes by which anemia develops; this in turn entails a discussion of normal blood formation.

PHYSIOLOGY OF NORMAL RED BLOOD-CELL FORMATION

The nucleated red blood cells, which are formed in the widely scattered bone marrow and which eventually enter the blood stream without nuclei, are the products of the integrated functioning of many body tissues. The red blood cell is composed in great part of hemoglobin, an active compound capable of a very large number of chemical exchanges with oxygen and carbon dioxide. The hemoglobin molecule is an extremely large one composed of protein, globin and iron-porphyrin — a pigment closely allied to chlorophyll. Thus in the formation of hemoglobin both protein and iron are essential substances, with the possibility that preformed pyrrole groupings derived from plants are also necessary. These substances are obtained only from food, which thus becomes the first of the important factors in normal hematopoiesis.

Diet. For hemoglobin formation the diet should at least contain adequate quantities of protein and iron. The exact protein requirement which is essential in the adult human being is not known, but it should be above 60 gm. and preferably above 80 gm. a day. Furthermore, from the standpoint of blood formation Whipple[1] has differentiated "good" and "poor" protein, the former being that of meat, fish, chicken, eggs and liver, the latter that of milk, cheese and legumes.

The protein constituent of the diet is intimately bound up with the "extrinsic substance" of Castle.[2] By experiments which by now are familiar to most physicians, this investigator showed conclusively that a substance in the diet (extrinsic factor) was acted upon by an element in the gastric juice (intrinsic factor), with the result that a third substance was elaborated which was essential for normal hematopoiesis. Its exact nature has not been completely established; it is present in meat, liver and eggs, and in foods rich in vitamin B. Its complete identity with this vitamin, as at first hypothecated by Strauss and Castle,[3] has been shown to be questionable, but there can be no doubt that there is some close relation between vitamin B and the extrinsic substance. The normal American diet, containing such foods as meat, fish, eggs and milk which are rich in protein, yields sufficient extrinsic substance for normal hematopoiesis.

The vitamin B complex, whether or not it is identical with the extrinsic factor, is probably an essential element in normal hematopoiesis. This food element, which consists of many unrelated nitrogen compounds, is present in relatively large amounts in animal muscle and organs, wheat germ,

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egg yolk, cereals, rye bread and certain of the green vegetables.

The iron requirement of man has not been completely worked out, chiefly because of the difficulty of doing complete iron balance experiments. However, several authors[4] have shown that the dietary intake of iron should be in the neighborhood of at least 6 mg. a day, although the optimal requirement is usually greater. This amount of iron is derived chiefly from the muscle fibers of meat, the yolks of eggs and the iron compounds of plants. The iron requirement at different stages of life probably varies considerably, that of the growing child being far greater than that of the adult; Blackfan[5] has estimated that the iron requirement of the former is 0.76 mg. per kilogram of body weight. The menstruating woman loses large quantities of iron at regular intervals and the iron requirement thereby becomes greatly increased. The beginning of menstruation in young girls may at times completely outbalance the normal iron stores in the body. The question of the optimal amount of iron in the diet is further complicated by such factors as the availability of a given type of iron compound and its utilization by the body. According to Witts,[6] "Not all iron compounds appear to be available for use, the available iron corresponding closely with the simple forms of iron. . . . Hemin derivatives do not give these reactions, and they appear to escape absorption in the alimentary tract."

There has been much debate concerning the place of copper as a factor necessary for hemoglobin formation. It would appear that this element is essential in normal rat hematopoiesis, where it acts as a catalyst in making iron available for hemoglobin production.[7] Whether the experimental results in rats can be carried over to human beings is debatable.

Thyroxin, which regulates the general metabolism, is probably also an essential element in red-cell formation. Vitamin C, which is necessary in so many oxidative mechanisms, also appears necessary for normal hematopoiesis. Other factors such as manganese, vitamins A and D, pituitary hormone and sex hormone have so far not been definitely related to the formation of red blood cells.

Gastric Juice. The constituents in the diet are acted upon by the gastric juice, which is dependent upon a normally functioning gastric mucosa. Among other materials, the normal gastric juice contains dilute hydrochloric acid, pepsin, rennin and a secretion (intrinsic factor) which Castle[2] discovered was important in the digestion of certain elements (extrinsic factor) in the diet. An acid medium is apparently the one most suitable for normal gastric digestion, although its presence is not absolutely essential.

Although no specific enzyme concerned with the liberation of iron from the complex compounds in which it is contained in food has been discovered, the free hydrochloric acid of the gastric juice is probably of greatest significance in this regard. Whether pepsin and Castle's intrinsic factor are of any significance in iron digestion is questionable, except perhaps indirectly in their effects on protein foods.

Protein as such is acted upon chiefly by pepsin and by Castle's enzyme (intrinsic factor). Meulengracht,[8] from dissection experiments on the stomachs of pigs, with subsequent feeding of this tissue to patients with pernicious anemia, demonstrated that the enzyme is produced in greatest concentration in the pyloric gland region of the stomach and duodenum. In this region, which extends along the lesser curvature of the stomach into the duodenum, and at times farther down the small bowel, the glands are identical anatomically and in all probability functionally. Their products result in a secretion which is active in the digestion of certain foods containing protein and vitamin B, the resultant combination being a substance which is apparently essential for the normal functioning of the bone marrow and the normality of the tongue, the gastrointestinal tract and the central nervous system. Thus, of all the organs in the body responsible for normal hematopoiesis none are of greater importance than the stomach, which may be called the keystone of the process.

Intestines. The constituents of the diet having been acted upon by the gastric juice, with the resultant formation of material necessary for normal bone-marrow function, they are then acted upon by the intestines. It is likely that further digestion of these substances continues in the bowel, but the most important intestinal function is probably that of absorption. The exact sites of absorption of the end products of gastric digestion remain obscure, but it is likely that absorption of iron compounds takes place in the small intestine, and that protein absorption probably takes place to the greatest extent in the large bowel. However good the diet and however adequate the gastric secretion, it is of course essential that the intestinal tract possess a normal absorptive capacity, thus allowing the withdrawal of substances into the blood and thence indirectly to the bone marrow.

Liver. It is becoming increasingly evident that the liver takes some part in either the final elaboration or the storage of hematopoietic substance. Its relation to blood formation has naturally been considered ever since liver substance was introduced as a therapeutic element in the treatment of ane-

mia, but definite proof was lacking until very recent years. Recent experiments of Wilkinson and Klein[9] and of Goldhamer, Isaacs and Sturgis[10] have shown that liver is potent chiefly because of its large store of substances that stimulate the bone marrow. It is possible that the liver may not only function as a storage reservoir but may be active in the final elaboration of these active principles, thus rendering them ready for utilization by the bone marrow. Aside from the liver, it is likely that the kidney, the brain and possibly other organs are of value.

The substances which finally result from the gastric digestion of dietary constituents, and which find their way to the bone marrow after circuitous routes in the intestines and liver, are then taken up by the growing cells of the marrow. With both liver-extract substance (maturation factor) and iron products present, the primitive erythrogone,[11] devoid of hemoglobin, gradually takes up this pigment in its cytoplasm, and the cell matures through successive stages until the nucleus becomes pyknotic and is discharged from the cell. This leaves a peculiar type of cell, without nucleus, in reality a bag containing hemoglobin, in readiness for the millions of chemical exchanges which take place until the cell is finally broken down.

ETIOLOGIC MECHANISMS IN THE DEVELOPMENT OF ANEMIA

The various mechanisms concerned in the development of anemia may be conveniently grouped as in the discussion of normal hematopoiesis.

Diet. Profound and continued deficiency of the various dietary factors must eventually lead to the development of anemia. This occurs, for example, in certain peculiar individuals who habitually loathe meat, fish, eggs and green vegetables, and subsist for many years on very little more than milk, toast, tea and possibly an occasional bit of herring. During the worst years of the depression many indigent families were unable because of cost to obtain those foods which contain the most iron — meat, eggs, green vegetables — and thus subsisted on a scanty iron ration. Inadequate diets are too often prescribed by the conscientious physician who, because of the finding of hypertension, arthritis or albuminuria, gives strict directions about avoiding meat, eggs and liver. The first-stage Sippy diet is notably poor in iron. Babies may be kept on the breast too long, or for various reasons be continued on a meatless, purely milk regime. In all these situations the body will gradually develop a state of chronic iron deficiency; the iron stores will gradually become depleted; and the skin, the mucous membranes, even the bone marrow itself will be called upon to make good this negative iron balance. Certain phenomena will then present themselves:[12] flabby, wrinkled skin; smooth, reddened tongue; dry, lack-luster hair, often prematurely gray; sores at the corners of the mouth; flattened fingernails; pallor; and hemoglobin deficiency in the blood. The blood cells continue to be produced in large numbers despite this insufficiency of iron. This must lead to a diminution of the hemoglobin in the individual cell, and finally to the production of small red blood cells. The anemia of iron deficiency is thus hypochromic and microcytic in type.

Protein deficiency as such without reference to Castle's extrinsic substance may lead to anemia, as suggested recently by Bethell,[13] but ordinarily a marked protein deficiency will result in loss of material necessary for liver-substance formation.[14] In the absence of extrinsic substance, characteristic and well-known phenomena present themselves: early graying of the hair, glossitis, gastrointestinal disturbances, central nervous system defects, and a peculiar state of the bone marrow which is reflected in the blood as an abnormality of the red blood cell, namely the macrocyte. Sufficient hemoglobin is present for the relatively few red blood cells which are being formed, with the result that a hyperchromic-macrocytic type of blood picture (pernicious anemia) develops.

We must emphasize that the bone marrow is not always implicated in these deficiency syndromes, and that anemia is therefore not always present. Deficiency in the vitamin B complex may lead to anemia, or to various dermatologic, gastrointestinal and central nervous system phenomena without associated anemia. Deficiency in vitamin C leads both to vascular defects (scurvy) and at times to changes in the bone marrow (anemia). Deficiency in vitamin D has led to no definitely characteristic form of anemia. In myxedema, which may be associated in certain cases with a lack of the substances necessary for thyroxin synthesis, anemia frequently develops.

Gastric Disorders. The diagnosis of gastritis, made so commonly many years ago, but recently held in ill-repute, has, in common with many other swings of the medical pendulum, again come into its own. This has been chiefly brought about by two outstanding advances: the development of the semiflexible gastroscope of Schindler[15] and the mucosal-relief, roentgen-ray studies initiated by Berg.[16] Both these have shown how commonly the stomach is involved with various types of inflammatory disorders which may finally lead to actual atrophy of the gastric mucosa. This atrophy may be either spotty or complete. The role of long-continued abnormalities of the autonomic nervous system or of congenital defects of the gastric mucosa in the production of atrophic gastritis is not yet understood. In the presence of this condition, however, both

hydrochloric acid and Castle's enzyme disappear from the gastric secretion. It has been shown that a deficiency in hydrochloric acid will interfere with the normal digestion of iron-containing foods,[17] and clinically the iron-deficiency state associated with achlorhydria has been abundantly recognized in the last few years.[18] Although it was at first felt that in pernicious anemia there was complete absence of the intrinsic factor, recent studies by Goldhamer, Sturgis and Isaacs[19] have shown that there is instead a diminution, which is sufficient with or without dietary deficiency to bring about the liver-extract-deficiency state known as pernicious anemia. Whether a deficiency state finally develops in a given case does not always depend upon a single factor. A number of individuals exposed to identical conditions of deficiency will not invariably develop the same state. Thus, in both the iron-deficient and the liver-extract-deficient states the abnormality of the gastric mucosa (and of the gastric juice) is probably only one of several abnormal etiologic factors. Many individuals are likely very little the worse for long-standing atrophic gastritis. If, however, for some reason such as infection, extraction of teeth or insanity, the diet becomes impaired, the *combined* effect of an inadequate diet and an inadequate gastric juice becomes evident as a deficiency state. Multiple factors may thus become essential for the development of a deficiency state in a given case. Castle[20] has expressed the situation in the form of an equation:

$$\frac{\text{Extrinsic factor} \times \text{Intrinsic factor}}{\text{Intestinal impermeability or destruction}} = \text{Liver extract}$$

Not only may idiopathic gastritis result in a deficiency state, but gross disturbances of the stomach as seen in extensive scirrhous carcinoma (linitis plastica), polyposis and gastrectomy will almost certainly lead to the anemic state.[21] Whether the resultant anemia will be microcytic or macrocytic probably depends upon a number of factors: diet, storage of essential substance, the presence of Brunner glands in the bowel and the status of the bowel itself. An interesting cause of the iron-deficiency state, emphasized mostly by English authors,[22] is associated with an improperly functioning or overfunctioning gastroenterostomy in which the whole bolus of food is unceremoniously dumped into the intestine without proper admixture with the gastric juice, and thus without adequate gastric digestion. Almost invariably these cases are associated with moderate to marked hypochromic anemia.

Intestinal Disorders. When intestinal absorption is greatly interfered with, as in chronic diarrhea, the products of the interaction of the food with the gastric juice are no sooner formed then they are removed. This must inevitably lead to a state of deficiency. Thus the so-called secondary anemia of chronic ulcerative colitis may at times be of the microcytic-hypochromic type, particularly in the active stage when bleeding is present, but a macrocytic (liver-extract-deficient) anemia may develop when the disease has been present for many months and atrophy or polyposis has occurred. The anemia of tropical or nontropical sprue, of chronic vitamin B deficiency states with diarrhea or of chronic regional ileitis is often of the liver-extract-deficient type. Despite the obvious etiology, this anemia is just as "pernicious" as pernicious anemia. Pernicious anemia — or better, liver-extract-deficiency syndrome — may thus be considered as the end result of various etiologic factors, whether these are single or multiple in a given case: dietary, gastric, intestinal and possibly hepatic.

Disorders of the Liver. In the last few years, with the publication of numerous papers on the macrocytic anemia of hepatic disease,[23] the liver has again assumed a large importance, some of it undoubtedly undeserved. In certain cases of cirrhosis of the liver the anemia may be macrocytic. Some authors claim that cirrhosis of the liver is almost always accompanied by macrocytic anemia, which is said to be identical with pernicious anemia. The slight reticulocytosis following injections of liver extract in a few of these cases has been cited as evidence. Recent observations of our own have shown that despite actual macrocytosis of the mature red blood cells, the bone marrow may differ entirely from that of pernicious anemia. The type of cellular growth is normoblastic, and not megaloblastic as in pernicious anemia,[11] and the mature red blood cells are probably larger because of some cytoplasmic disturbance differing completely from the essential abnormality of the nucleated red cells in pernicious anemia. That the anemia of most cases of hepatic disease is a liver-extract-deficiency state is very much to be doubted, although it cannot be denied that in certain instances of severe cirrhosis of the liver the combination of anorexia, nausea and vomiting and of intestinal and hepatic disturbance may together result in loss of liver-extract substance and thus in a specific type of macrocytic anemia.

Other Abnormalities. Abnormalities of the diet, the gastrointestinal tract and the liver involve the marrow indirectly through interference with various maturation factors of the marrow cells. In certain other conditions the marrow is directly attacked by a pathologic process. This occurs as the result of the action of certain chemicals (arsenic, benzol, radium, radioactive substances, x-ray and

gold) which destroy the marrow and produce an aplastic anemia. Carcinoma, lymphosarcoma, Hodgkin's disease and most cases of leukemia show invasion of the marrow cavities by the abnormal tissue, and much more commonly than is suspected. This interference with growth processes will eventually lead to anemia, leukopenia and thrombocytopenia. At least half our cases of leukemia have been associated with a low white cell count.

There are some conditions in which, although all the physiologic processes under discussion are in good order, anemia is nevertheless present. The most obvious of these is acute hemorrhage, with its attendant loss of large quantities of hemoglobin. That severe anemia may result from the continued loss of minute quantities of blood is frequently not appreciated. In pregnancy, all the processes of digestion, diet and bone-marrow function may at the outset be normal, and yet because of certain hypothetical toxic substances elaborated by the fetus, or because of its actual removal of necessary blood-building substances, anemia may result.

So far, only those conditions associated with abnormalities in the formation of blood cells have been considered. A few rather unusual and still idiopathic conditions are present which show an increased degree of red blood-cell destruction: congenital hemolytic anemia, sickle-cell anemia, erythroblastic anemia and erythroblastosis of the newborn. It is not known whether the increased cell destruction in these conditions is due to actual abnormality of the cell-destroying tissue (the reticuloendothelium) or to congenital abnormalities of the red cells themselves, making them an easy prey to destruction. Certain recent work, particularly that of Haden,[24] suggests that the abnormality in congenital hemolytic anemia is a hereditary defect of the red blood cell itself (spherocytosis), in which thicker, more globoid cells are produced, more fragile than normal and thus more readily destroyed.

Although the etiologic factors in these conditions have not yet been discovered, it is probably undesirable to call the anemia primary. Until its mechanisms have been worked out, it is best to reserve opinion.

GENERAL PRINCIPLES OF TREATMENT

In recent years there seems to be a growing tendency to treat almost every case of anemia with a mixture of iron, liver and vitamin B, on the theory that none of the ingredients can do harm, whereas one or several may do good. Frequently, it appears, there is no great concern about exact diagnosis. The proper treatment of a case presenting anemia demands not only all one's faculties of diagnostic acumen but a thorough knowledge of the physiologic principles involved in the production of anemia. To be more specific, if one is confronted with a case presenting anemia what are the things to be done?

First, there is the history. Particular attention, aside from the routine questions, should be paid to early graying of the hair, a "burning" tongue, sores about the angles of the mouth, gastrointestinal symptoms, brittle fingernails, paresthesias of the fingers and toes, difficulty in walking, chronic blood loss and above all the diet. The food intake, meal by meal, should be inquired into minutely, with particular reference to meat, fish and green vegetables. Pains in the bones, fever or black and blue spots may be indicative of bone-marrow involvement by leukemia, Hodgkin's disease or metastatic carcinoma. The occupational history is of utmost importance from the standpoint of chemical injury of the marrow. The history, by focusing attention on the diet, the gastrointestinal tract and the presence or absence of known bleeding, should lead one to suspect most of the etiologic factors present. The physical examination may lead one into all kinds of interesting byways. Is there icterus? What is the status of the reflexes and of the vibration sense? Is the heart involved? Do the retinal blood vessels show albuminuric retinitis? Is there an abdominal mass? Is the spleen enlarged? Is there lymphadenopathy? Are there evidences of platelet deficiency in the form of ecchymoses and petechiae? From the standpoint of examination of the blood, most important is determination of the type of anemia present. Is it macrocytic, normocytic, microcytic or hypochromic?

The complicated classifications for anemia used in the past have to great extent been superseded in recent years by one based on cell size. Although this too is not completely satisfactory, its value may be enhanced by combining with it an etiologic suffix, in this manner:

Macrocytic anemia:	inadequate diet, impaired gastric digestion.
Microcytic anemia:	inadequate diet, multiple pregnancies in the past, menorrhagia.
Normocytic anemia:	benzol poisoning.

This classification has been found extremely useful: knowledge of the cell size frequently throws light on the probable etiologic, diagnostic and prognostic possibilities; listing the possible etiologic factors is a reminder that the anemia is secondary to various causes which must be thoroughly investigated.

The cell size may be determined in various ways: by estimation from a well-made cover-slip blood smear; by the color index; by actual measurement of the red-cell diameters with a micrometer eyepiece (Price-Jones[25]); or by determination of the

mean corpuscular volume from the relation between the hematocrit and the red cell count (Wintrobe[26]). All these methods have their place; in a doubtful case they should all be utilized. Knowledge of the cell size often carries one a long way to the final diagnosis, for if the anemia is microcytic the bone marrow is probably not seriously involved. If it is macrocytic, either a liver-extract deficiency state is present or the bone marrow is involved by a leukemic or malignant process. If it is normocytic, bone marrow involvement must again be considered, together with such possibilities as nephritis, myxedema and various chemical injuries to the marrow. Hypochromic anemia is therefore usually benign in its implications, whereas the reverse is true of macrocytic or normocytic anemia, unless pernicious anemia and myxedema can be diagnosed. A fairly complete index of the status of the bone marrow may be obtained from careful study of the leukocyte count, polymorphonuclear percentage, percentage of immature granulocytes, reticulocyte percentage and platelet count. The differential count of the white cells is, to be sure, all-important in the diagnosis of leukemia, whether leukemic or aleukemic.

In some cases various special laboratory tests may be essential: gastric analysis, examination of the stool for occult blood, gastrointestinal roentgen-ray examination, icterus index, fragility test and x-ray examination of the bones. If the diagnosis remains obscure even after these investigations, a sternal bone-marrow biopsy may solve the problem.

Once the diagnosis of a case with anemia has been worked out and the various etiologic factors evaluated, treatment is either relatively easy or difficult if not hopeless.

TREATMENT OF THE IRON-DEFICIENCY STATE (HYPOCHROMIC ANEMIA)

The iron-deficiency state known for many years as secondary anemia, more recently as hypochromic anemia (with or without the prefix "primary," "achlorhydric," "idiopathic," and so forth), is most readily treated with iron.

Iron therapy has passed through several well-defined cycles. In the days when chlorosis was a common disease (1870-1910), most authorities advocated small doses of the metal, although von Noorden[27] advocated prescribing 100 mg. of actual iron per day. This was usually obtained from Blaud's pills, each pill containing 20 mg. of actual iron. Reduced iron in 1- to 4-gr. doses daily, oxidized ferrous sulfate and tincture of ferric chloride were also used. Gradually smaller doses of iron began to be used, possibly on account of the warnings of several clinicians regarding the toxic qualities of iron preparations. Thus Williams[28] in 1882 concluded that metallic iron had "poisonous qualities," and was even skeptical of the "tonic" properties of the metal. Bunge,[29] a well-known German clinician of the time, felt that the action of inorganic iron in chlorosis was more in the mind of the physician than on the patient. It must be realized that in this period (1880-1890) so few estimations of the hemoglobin concentration and counts of the red blood cells were made that these were considered worthy of note in our local journal. With the gradual wane in the frequency of chlorosis, treatment with iron was common although not the subject of much comment, but with the advent of the new idiopathic or primary hypochromic anemia and its recognition as

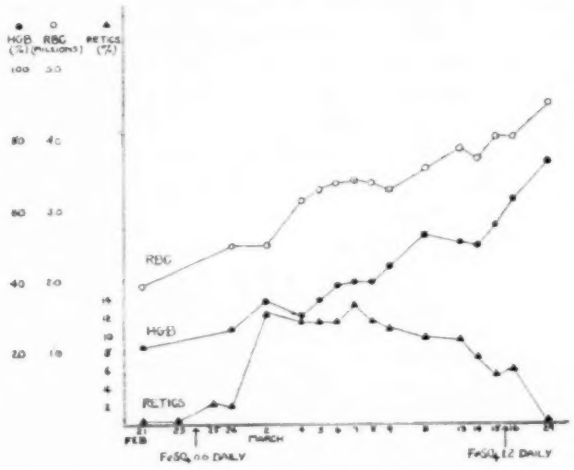

Chart 1. *G. C. Chronic hypochromic anemia treated with ferrous sulfate. Note the well-marked reticulocyte response (maximum 13.2 per cent), the rapid increments in hemoglobin and erythrocyte values, and the secondary rise in percentage of hemoglobin when the dose of ferrous sulfate was doubled. Optimal dosage with this drug is usually from 0.8 to 1.0 gm. (12 to 15 gr.) daily.*

a state of iron deficiency (about 1930), together with the knowledge that maximal doses of liver were effective in pernicious anemia, various clinicians began to use relatively enormous doses of iron in these cases. Thus, Minot[30] in 1929 advocated the use of the soluble iron salt, iron and ammonium citrate, in dosage of 3 to 6 gm. (45 to 90 gr.) daily, and Schulten[31] in 1930 advised giving 6 gm. of reduced iron daily. Dameshek[32] in 1934 concluded, on the bases of reticulocyte and hemoglobin responses to various types of iron compounds, that to obtain maximal effects it was necessary to give doses of actual iron averaging 1000 mg. However, in the last few years so rapidly has the kaleidoscopic picture of anemia been shifting that one is forced to modify this statement. Although small doses of ferrous iron had been in

use for many years, it was not popularized until ferrous chloride,[33] ferrous glutamate[32] and later ferrous sulfate[34] were introduced or reintroduced into clinical practice. The most popular form of ferrous iron in this country has proved to be the latter drug, which is given in dosage of 1 gm. or less per day. It is essential that the ferrous sulfate be so prepared that it cannot be oxidized to the ferric form, this being ordinarily accomplished by the use of a special coating. Maximal response may frequently be obtained by the use of less than 1 gm. daily (Chart 1). Only occasionally is it necessary to give more than this, and in only one case within the last year has the drug been relatively ineffective (Chart 2). In this case of relapsing chronic hypochromic anemia, there was no response to ferrous sulfate even in double the ordinary dosage; iron and ammonium citrate, however, when given first in 3-gm. then in 6-gm. doses, produced a maximum response.

In contrast with the frequent gastrointestinal symptoms complained of when iron and ammonium citrate was used (noticeable in about one third of the patients) the lack of reactions with ferrous sulfate is indeed striking. Diarrhea does not occur; in fact a slight degree of constipation may result. In most cases there is no complaint of gas, distress, belching or nausea. So striking, indeed, is this lack of reaction that when it occurs one should suspect the possibility of a gastric lesion, especially neoplasm. This was recently brought out in three patients who because of the presence of hypochromic anemia were given ferrous sulfate without further investigation. All three complained of severe distress and nausea, and when examined by gastrointestinal x-ray were found to have carcinoma of the stomach.

A few cases are refractory to iron treatment. If such possibilities as malignancy, chronic infection and hemorrhage have been ruled out, the dosage of iron should be doubled or even tripled. If with extremely large dosage of ferrous sulfate the response is still inadequate, iron and ammonium citrate may then be tried in from 3- to 6-gm. doses. I have rarely found it necessary to use copper. That it has an effect in some cases of hypochromic anemia refractory to iron treatment cannot be doubted from previous studies in a group of cases treated with a copper-free iron preparation.[32] In about 75 per cent of these cases maximal responses followed the use of iron alone, and in the remainder small doses of copper sulfate (.005 gm. daily), given with the iron, were effective in continuing the hemoglobin response. That a combined copper and iron deficiency is occasionally present is possible, but this does not warrant the routine use of copper in hypochromic anemia, particularly in infancy, where routine treatment with copper has been actively advocated. The end results of copper storage, presumably by the liver, have not yet been demonstrated, but Mallory's investigations[35] lead one to suspect the possibility of future hemochromatosis. At the present stage of our knowledge, therefore, we shall do well to refrain from the use of copper unless it seems essential to increase the hemoglobin concentration in a case of hypochromic anemia refractory to all types of iron treatment.

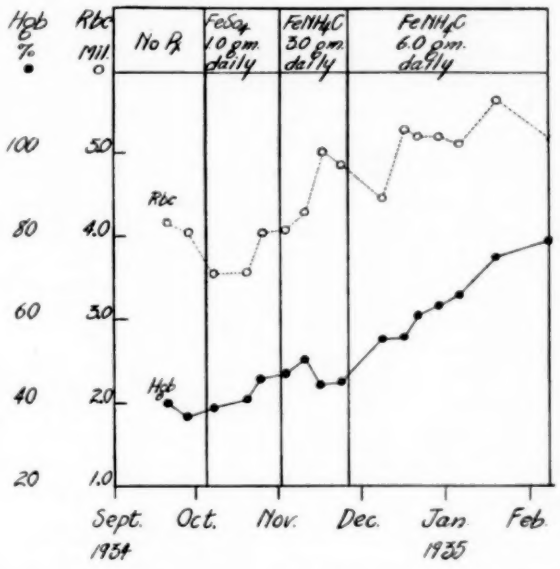

Chart 2. *B. S. Chronic hypochromic anemia. Note the comparative lack of response to 1 gm. ferrous sulfate and 3 gm. iron and ammonium citrate daily. A satisfactory rise in hemoglobin occurred when large doses of iron and ammonium citrate (6 gm. daily) were given. Most cases, however, respond as well to relatively small doses of ferrous sulfate as to large doses of iron and ammonium citrate.*

Liver or liver extract is rarely necessary in the treatment of hypochromic anemia unless a combined deficiency of iron and liver is present. This occasionally occurs in cases of pernicious anemia bleeding from various causes, and rarely in states of extreme dietary and gastric deficiency. In most cases the results obtained by iron alone are maximal. To add liver extract is not only useless but wasteful of the patient's finances. The various commercial mixtures of iron and liver extract probably have no more value than their contained iron, which is frequently much less than the optimal dosage. It is true that a prescription for the preparation "Fancy Name A" may often be more impressive to the patient than one for a simple iron salt, but we should impress patients in a more rational fashion. We should warn them against the large numbers of "shotgun" preparations for anemia which fill the druggists' shelves. These contain

iron, liver, vitamins A, B, C, D and so on, together with some accessory metals as manganese and copper. We are now passing through a most active "vitamin cycle," and to prescribe iron or copper or liver without vitamins is to be not quite modern. The exact necessity of treatment with large doses of the several vitamins in cases of hypochromic anemia is very doubtful. Maximal results are obtained from the exhibition of one drug alone — iron.

During the progress of treatment, investigation into the various causes which have led to the state of iron deficiency should be continued and efforts made to correct them one by one. The dietary habits of a lifetime are frequently hard to break, and it is only by long training and persuasion that we can finally make some of these patients resume a normal, balanced diet. These efforts are distinctly worth while, however, from the standpoint of prevention of relapses, which may be just as frequent as in pernicious anemia, and it is sometimes necessary, especially in the completely idiopathic cases, to continue permanently a small dose of iron daily, namely 3 gr. (0.2 gm.) of ferrous sulfate or 7.5 gr. (0.5 gm.) of iron and ammonium citrate.

Special note should be made of the treatment of severe degrees of chronic hypochromic anemia prior to extensive operative procedures. The operative mortality in cases of peptic ulcer which have bled and in cases of carcinoma of the stomach with marked anemia may be materially altered by adequate preparation of the patient prior to operation. The period of preparation may well take from two to four weeks; this may be distinctly worth while, since filling the tissues and blood with adequate concentrations of hemoglobin may mean the difference between a successful and an unsuccessful operative result. Preparation of the patient is made by the use of several blood transfusions given at intervals of from two to four days, and by the use of iron in sufficient dosage. A maximal response to iron medication is obtained in about a month. With the use of transfusions, this period may be shortened by one or two weeks.

Hypochromic anemia of slight degree almost invariably results during the course of pregnancy, in all probability owing to the loss of iron stores to the developing fetus. The prophylactic administration of iron in pregnancy has been advocated,[36] and it is probably true that it cannot do harm and may be of distinct value in the occasional pregnant woman who, by virtue of poor diet or a disturbed gastric function, might have developed an iron-deficiency state. So far, the general use of parenteral liver has not been advocated.

With overstuffed iron stores in the mother, the likelihood of anemia's developing in the infant is extremely remote. This occasionally happens, however, when infants are kept on the breast too long, or if milk-fed are not given meats until after the first year of life. Good pediatric practice now requires meat and green vegetables to be given after the first few months; the "milk anemia" of former times was an iron-deficiency state brought about by continued lack of iron in the diet. Treatment is simple, and may be accomplished by the use of iron and ammonium citrate in the bottle feedings or by saccharated oxide of iron.

TREATMENT OF THE LIVER-EXTRACT-DEFICIENCY STATE (PERNICIOUS ANEMIA)

In 1872, Biermer first described a group of cases distinct from chlorosis; because of their fatal character, he called them progressive pernicious anemias. The first article[37] on anemia published in the *Boston Medical and Surgical Journal* (1876) dealt with the report of a case. The red cells were, however, described as being smaller than normal. This fact, together with the large number of ecchymoses present, makes one suspect an error in the diagnosis. The second article on anemia was a case report by Dr. G. B. Shattuck;[38] he said that "the phrase 'progressive pernicious' is mainly objectionable if it is supposed to imply a necessarily fatal outcome; the term 'idiopathic' ceases to be applicable as soon as we get some clear idea of the cause or causes which undoubtedly exist." Thanks in great part to work which has emanated from our own city, the disease is no longer pernicious, and neither is it idiopathic. The vague term "liver-extract-deficiency state" may perhaps be more suitable than the outmoded term "pernicious anemia," since it does not stress the anemia which at times is slight, even though manifestations referable to the central nervous system may be well marked. In reality, the disease is a syndrome which is the end result of numerous factors which may operate differently in various cases. The dietary factor, so striking in some cases, may be minimal in others and the same holds true for the gastric, intestinal and hepatic factors. Whatever the various causes, when the body becomes insufficiently nourished with the liver-extract principle various ectodermal structures such as the skin, hair and tongue suffer, the central nervous system usually becomes impaired, and the bone marrow becomes markedly involved. The anemia is simply a secondary manifestation of bone-marrow involvement. In treatment, however, the status of the blood must assume major significance, because it is a yardstick invaluable in the analysis of our therapeutic results.

In treating the liver-deficiency state we are faced

with an embarrassment of riches, whereas prior to 1926 we had nothing. The decade since the introduction of liver treatment has been one of the most crowded and fruitful ones in the history of medicine. It may fairly be said that as the result of the success of liver treatment have come directly or indirectly thousands of researches and a tremendous interest in what was once a comparatively neglected field, that of the blood. In these crowded years have appeared in rapid succession liver, liver extract, gastric substance, combinations of liver with gastric tissue (extralin), liver extract in solution, autolyzed liver and finally many types of liver extract for parenteral use. The physician who has discovered a patient with pernicious anemia is faced not with the problem of "What shall I do?" but with the much more pleasant one of "What preparation shall I give?"

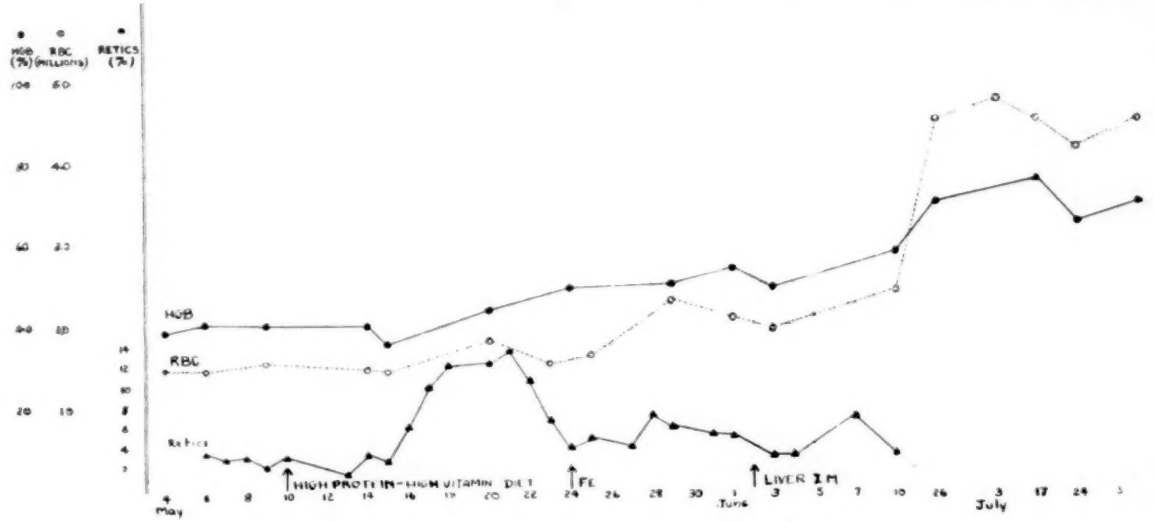

Chart 3. *E. S. Pernicious anemia. This chart illustrates the mixed character of the deficiency state in certain cases of pernicious anemia. The well-marked reticulocyte response to a high-protein diet without liver indicates a dietary deficiency (which was marked); the slight reticulocytosis to iron and the definite increase in hemoglobin percentage indicate a certain degree of iron deficiency. Liver extract finally induced a striking remission in the red cell count.*

The parenteral preparations have appealed to most physicians as being the most valuable for general use. Three years ago, Castle and the writer[39] demonstrated by the method of the double reticulocyte response the great differences in potency of the various extracts, and pointed out that the vital question is not what the extract is derived from but how much active material is present in the vial ready for injection. As a result of this and other work, the phrase on the vial of liver extract for parenteral use, "Derived from so and so many grams of liver," has been abandoned, and in substitution an arbitrary unit has been established.[40] The unit as now defined by the Council on Pharmacy and Chemistry of the American Medical Association is the least amount of material which when injected daily during a ten-day period produces a standard reticulocyte response. Determination of the relative potency of various products is extremely difficult, for there is as yet no crystalline product available, and furthermore no test using the experimental animal has proved completely satisfactory. There is much discussion regarding the relative merits of the dilute versus the concentrated extracts. In the Blood Clinic at the Beth Israel Hospital we have been using both dilute and concentrated products of several manufacturers and have compared them by weekly administration for separate three-month periods with a small group of from ten to twelve patients. This work instead of clarifying the issue has at times confused it. A dilute extract in one patient appears to give better results than a concentrated one, yet the reverse is true when the same extracts are used in another patient. What is more, the status of the red cell count and hemoglobin does not always give the whole story; in patients with well-marked central nervous system involvement, slight fluctuations in the red cell count are of little significance as compared with changes in the reflexes and the vibration sense. There can be no question that much loss of potency takes place in the process of concentration and refinement; this is compensated for, however, by the fact that a large number

of units can be given in a relatively small injection.

The weekly observation of this group of patients for a period of several years has thus far resulted in the following tentative conclusions: (1) that the counts of patients fluctuate considerably (relapses); (2) that in most cases it is necessary to give weekly injections for adequate maintenance; (3) that in some cases the more concentrated extracts are superior to the dilute in the control and amelioration of both the red cell count and the central nervous system manifestations; (4) that the various extracts have greatly varying potencies; (5) that certain extracts tend to cause a relatively high percentage of reactions, where others only rarely give reactions.

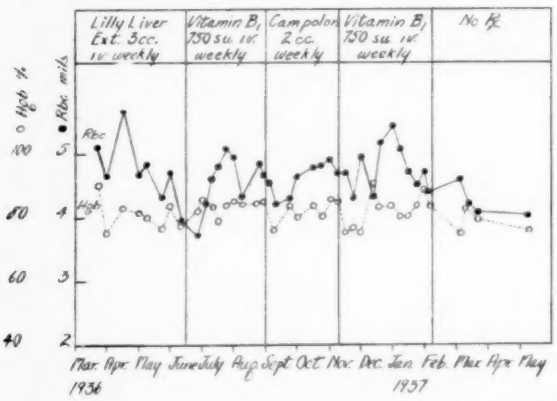

Chart 4. *J. A. Pernicious anemia. A case somewhat refractory to parenteral liver extract and with severe dietary deficiency. Vitamin B₁ intravenously in two periods was apparently effective in causing a definite elevation in the red cell count.*

There can be no doubt of the frequently reiterated statement that no exact rule can be formulated of the amount of liver extract which should be given in an individual case. The amount varies greatly; enough should be injected (1) to keep the symptoms under control, (2) to reduce the objective phenomena (tongue, central nervous system, and so forth) to a minimum and (3) to keep the red cell count up to a level from 4,500,000 to 5,000,000.

The central nervous manifestations must be treated with extreme vigor, often without reference to the hematologic changes. Our best results have been obtained by the use of a very large dosage of a fairly concentrated extract, given at the beginning as often as every day for a period of several weeks, followed by injections every two days and then twice weekly. Our results with the dilute extracts in these cases have not been nearly so good as those obtained with the concentrated products. Not only does parenteral liver extract stay the progress of the disease, but there can be no doubt of the striking changes in the sensory disturbances (vibration sense, hypesthesias, ataxia), and at times even in the reflexes, which occur when massive dosage is given. In two cases with slight to moderate optic atrophy, the improvement in vision and in the appearance of the optic disk following treatment with parenteral liver was striking. In general, it may be said that the sensory disturbances improve first and best, and those symptoms referable to the lateral columns improve most slowly.

Reactions to parenteral liver therapy are occasionally seen. Some extracts appear to give histamine-like reactions: marked flush and headache. Occasionally, chills and fever ensue. In one case it was necessary to discontinue parenteral liver on account of a generalized and stubborn skin eruption which occurred on two occasions after the first or second injection. Several patients complained of a badly swollen arm, and in one case it was necessary to discontinue injections because of the severity of the local reaction, which was accompanied by slight fever. One patient given injections of horse-liver extract developed severe reactions: chill, fever, nausea and vomiting; on questioning, it was found that she had had diphtheria antitoxin a few years previously. The reactions which develop are probably the result of hypersensitivity to the nitrogenous substances present, and can be obviated by one of several methods. Since most of the extracts are made from pig liver, one can shift to a beef-liver extract (Campolon, Winthrop) or to a horse-liver extract (Chappell). Other changes in the type of animal extract can be made as indicated. The method of desensitization may be employed. This was done successfully in three cases by giving very small doses (0.2 cc.) of the extract and gradually increasing the dosage to the desired maximum.

Accessory factors are rarely necessary in treating the liver-extract-deficiency state. When it is noted that the red cell count has outstripped the hemoglobin concentration and the color index is thus reduced to definitely less than 1.0, iron may be given. In one of our cases (Chart 4), that of a woman who for years had subsisted on an extremely deficient dietary, the addition of large doses of vitamin B₁ intravenously appears to have resulted in definite effects on the tongue, the gastrointestinal tract and the blood.

The pernicious anemia of pregnancy, despite liver extract, remains pernicious, requiring the utmost care in therapy. Most cases are apparently not recognized until late in the disease, when the red cell count has diminished to about 1,000,000. Because of the severe vomiting usually present, the diagnosis of toxemia of pregnancy is ordinarily made. By the time the possibility of a blood

dyscrasia is considered the patient may be almost moribund. Because the anemia is so refractory to liver therapy, one wonders whether the pregnancy has in some way interfered with the processes of utilization of liver factor (achrestia). In addition to enormous dosages of parenteral liver extract,

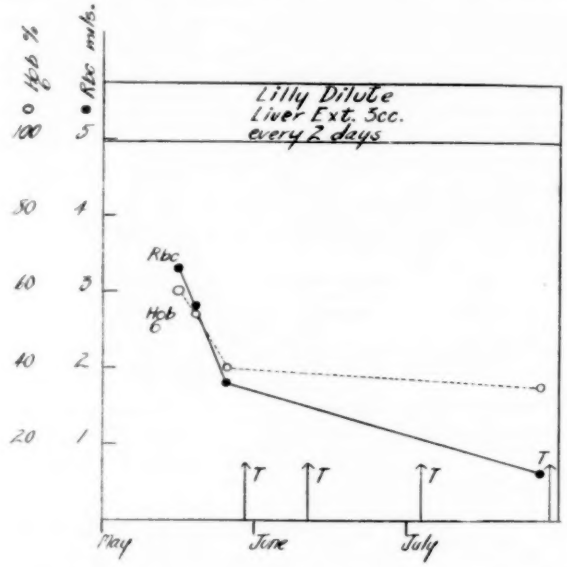

Chart 5a. *B. D. Pernicious anemia of pregnancy. The anemia was discovered in the eighth month of pregnancy. The course was progressive, despite dilute liver extract, transfusions (T) and interruption of pregnancy.*

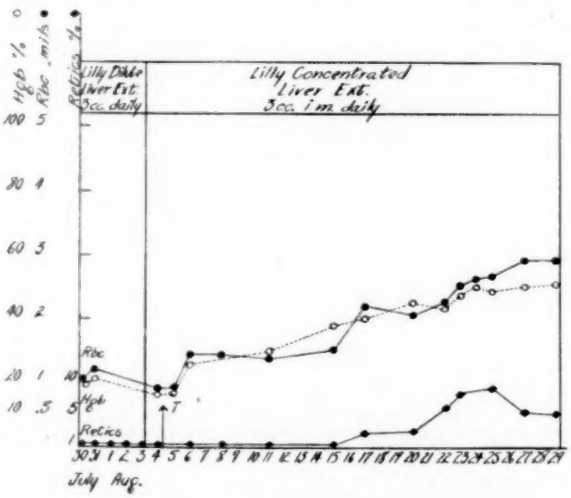

Chart 5b. *B. D. Further course. Although there was a lack of response to daily injections of dilute liver extract, gradual improvement without definite reticulocytosis occurred when daily dosage of a concentrated liver extract was given. The pernicious anemia of pregnancy is exceedingly refractory, possibly because of the lack of ability to utilize liver extract.*

transfusions of blood must ordinarily be given. Two cases seen within a month of each other had failed to respond to dilute liver extract given in 3-cc. doses every two days; when concentrated extract in from 3- to 6-cc. doses was given daily, a very gradual response took place within four weeks. Despite the low red cell count, definite reticulocytosis did not occur. Both cases made complete recoveries. In another case, death ensued despite large dosage of parenteral extract. In a fourth case, death resulted from a severe transfusion reaction accompanied by suppression of kidney function. In a fifth case, the anemia was discovered during pregnancy, and was controlled by large doses of parenteral extract given weekly during the last five months of gestation. When severe vomiting is present and pallor becomes evident, the possibility of pernicious anemia of pregnancy should be considered, and a red cell count done. A Tallqvist hemoglobin estimation is worthless.

TREATMENT OF OTHER CONDITIONS ASSOCIATED WITH ANEMIA

It must not be supposed that all cases with macrocytic anemia are examples of liver-extract deficiency and therefore amenable to specific therapy. To be sure, macrocytosis and macrocytic anemia are seen most strikingly in pernicious anemia, but they occur in other conditions with sufficient frequency to warrant discussion. A partial list of the conditions in which macrocytic anemia has been seen is as follows: the aleukemic leukoses, aplastic anemia, malignancy metastasizing to the bone marrow, splenic anemia, cirrhosis of the liver, pancreatic disease, acute and occasionally certain cases of chronic hemolytic anemia, chronic nephritis, and myxedema. The blood picture in some of these conditions is often so much like that of pernicious anemia that it cannot be distinguished from it. The great diagnostic and prognostic import of the triad, macrocytic anemia — leukopenia — thrombocytopenia, has gradually become recognized. In most cases this combination spells actual bone-marrow disease or destruction. The diagnoses which are made when these findings present themselves are varied, and frequently depend upon what part of the blood picture is stressed. Thus, with anemia outstanding, aplastic anemia, pernicious anemia, splenic anemia are diagnosed; with leukopenia, agranulocytosis, typhoid fever, undulant fever are considered; and when purpura due to platelet deficiency is found, the diagnosis of purpura hemorrhagica is usually made. The macrocytic anemia of hepatic disease has already been mentioned.

Because of their failure to respond to specific therapy, it becomes essential to distinguish these states of anemia, leukopenia and thrombocytopenia from pernicious anemia. No amount of treatment with liver extract will cause them to budge from their level of anemia, which in fact gradually becomes more severe. In most of these

cases the disorder is due to encroachment of normal marrow tissue by rapidly proliferating cells, usually leukemic, at times due to metastatic malignancy (lymphosarcoma, carcinoma), at times due to fibrosis. The diagnosis in many of these cases has been made through the use of the sternal bone-marrow biopsy, which has revealed either the presence of aplasia, leukemic proliferation or metastatic malignancy.[41] In certain cases the bone-marrow biopsy has been helpful in ruling out these states and has indirectly led to a diagnosis of hemolytic anemia, with resultant cure by splenectomy. The important thing is to recognize that there are conditions with macrocytic anemia not due to liver-extract deficiency, and that from the prognostic standpoint the triad, anemia — leukopenia — thrombocytopenia, is often indicative of serious bone-marrow disease.

THERAPY OF VARIOUS IDIOPATHIC CONDITIONS

In aplastic anemia — due to destruction of the marrow by various chemicals — liver and iron are valueless; transfusions should be given until the patient either recovers or shows no indication of any improvement. In cases of chronic hemolytic anemia, as a rule congenital, the value of splenectomy has been well substantiated. Recent studies have indicated that the defect in the congenital cases may be a hereditary malformation of the red blood cells, which are more spherical than normal and therefore more readily broken down by the reticuloendothelial system. Splenectomy is of therapeutic value, probably because it removes the largest single aggregation of reticuloendothelial cells in the body. In the so-called splenic anemia (Banti's disease), splenectomy is of doubtful value, although opinion on this point differs considerably. Space does not permit adequate discussion of the treatment of many other types of idiopathic anemia.

TREATMENT OF "TALLQVIST ANEMIA"

Anyone who sees a fair number of cases with anemia will not infrequently be confronted with the case of an individual, usually a woman of neurotic temperament, who has been told that her symptoms of weakness and lack of energy are due to anemia. The diagnosis has invariably been made by the referring physician on the basis of an estimation with the familiar Tallqvist lithographed scale, which has usually given a hemoglobin reading of between 60 and 70 per cent. Inspection of the palms and the mucous membranes leads one to suspect that the hemoglobin percentage is probably much higher, and this is confirmed when the Sahli hemoglobinometer is used. "Tallqvist anemia" seems to be fairly prevalent, and because it is the cause of much unnecessary medication, both oral and parenteral, deserves a word of comment. The Tallqvist scale as a measure for hemoglobin estimation is completely unreliable, especially in the range between 60 and 140 per cent.* Many Tallqvist scales seem to give average readings of about 70 per cent. I have found it good policy to discard this scale completely; if a rough estimate is desired, comparison of the patient's palms with those of the physician is usually more accurate. However, if greater accuracy is desired, the Sahli method offers this without undue complexity. The Dare hemoglobinometer, although very impressive in appearance, has been found to be extremely inaccurate. "Tallqvist anemia" is therefore best treated by discarding the Tallqvist scale and substituting for it a more reliable method of hemoglobin estimation.

SUMMARY

1. Anemia is always symptomatic of some underlying abnormality, whether this is dietary, gastric, intestinal or due to actual destruction of blood-forming tissue. In any study of anemia, the terms "primary" and "secondary" are best replaced by designations based on possible etiologic factors.

2. The anemia of a given case may be classified on the basis of cell size, which, together with a listing of etiologic factors, provides features of diagnostic, prognostic and therapeutic value.

3. The treatment of a case with anemia loses its frequent cut-and-dried character when proper account is taken of the abnormal physiology. This in turn entails some knowledge of normal hematopoiesis.

4. The importance of multiple etiologic factors leading to an iron-deficiency or a liver-extract-deficiency state is stressed, and present methods of treatment for these conditions are outlined.

*I have in my records the case of a physician with polycythemia who was treated for hypochromic anemia with large doses of iron because of Tallqvist readings between 60 and 70 per cent. The correct reading (Sahli) was between 107 and 114 per cent, with a red cell count 7,000,000.

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Discussion

THE CHAIRMAN: The discussion will be opened by Dr. Clark W. Heath.

DR. CLARK W. HEATH, Boston: In discussing Dr. Dameshek's excellent paper I wish to emphasize again some of the important aspects of the problem. Although there are now many preparations which are potent in the treatment of certain kinds of anemia, there is continuous misuse of them. This is partly due to a misconception of the manner in which these preparations act. Liver extract in the treatment of pernicious anemia, and iron in the treatment of hypochromic anemia, are substances which are supplying a deficiency. They do not, in the old sense, "stimulate" the bone marrow to put out more red blood cells or more hemoglobin. They supply material which is lacking in the body, and which, when provided, will result in normal maturation of red blood cells and normal hemoglobin formation. This is substitutive therapy. In the case of iron, the substitutive therapy has been shown to have a quantitative basis: the amount of iron assimilated may be recovered quantitatively in the newly formed hemoglobin.

Correct diagnosis is of extreme importance. Without a careful history and blood study, pernicious anemia can easily be confused with idiopathic hypochromic anemia, and vice versa. Iron will be without benefit in pernicious anemia uncomplicated by iron deficiency. Liver extract will be without benefit in iron deficiency uncomplicated by deficiency of the substance potent in pernicious anemia.

Pernicious anemia is almost invariably a lifetime disease. Early diagnosis and the early placing of the patient on a suitable regime which will maintain health are therefore important. The diagnosis is often confirmed by the results attained after the administration of a potent liver extract, and a potent liver extract alone. "Shotgun" preparations, containing several substances potent in different kinds of anemia, are to be condemned, especially in early care.

For a number of years I have been convinced that iron deficiency in adults is primarily the result of blood loss, often occurring in a subtle and chronic form, for example, chronic menorrhagia or bleeding hemorrhoids. Some cases are also the result of repeated pregnancies and prolonged lactation. Poor diet may play an important secondary role, but cannot alone produce iron deficiency. Careful history-taking and observation may reveal, in cases of hypochromic anemia, some bleeding lesion of the gastrointestinal tract of more importance than the anemia itself, for example, carcinoma of the stomach. In such a case iron therapy will usually benefit the patient, but this alone will not fulfill our duty to him. In the absence of blood loss, some cause for anemia other than iron deficiency must be sought. Myxedema will be treated unsuccessfully with iron or liver extract, but relief of the anemia is obtained by the administration of thyroid. Chronic hemolytic anemia will be treated unsuccessfully with iron or liver extract, but splenectomy may be curative. Anemia is often more a symptom than a disease, and the primary method may be treatment of the disease producing the anemia.

Disease of the blood-forming organs will always be an important problem of internal medicine. Complete aware-

ness of the significance of anemia, together with complete knowledge of the use and limitations of therapeutic agents, will always be necessities for the practitioner of medicine. The subject in one form or another is upon the program of every important general medical meeting. I trust that it will continue upon the programs of the Massachusetts Medical Society, and in such able presentations as the one we have heard today.

THE CHAIRMAN: Dr. Minot, would you like to give us a few words on this subject?

DR. GEORGE R. MINOT, Boston: There is little I can add to the presentation. There are some aspects of the subject that Dr. Dameshek did not refer to, but with which I realize he is well acquainted. If there is a recognized cause for a deficiency, such as recurrent loss of blood leading to iron deficiency, the condition should be removed if possible. It must be borne in mind that infection and severe damage to vital organs act to inhibit the utilization of iron, liver extract, vitamins and certain other dietary factors. In the presence of infection the individual must have a greater amount of such substances than when infection is absent. Many cases have not received enough iron or liver material because of failure to recognize not only that more is needed when infection is present, but also that optimal doses for different cases vary considerably.

In regard to doses of iron, Sydenham used doses of the size used today, and similar doses were used in the early part of the nineteenth century. In the *New England Journal of Medicine and Surgery* from 1812 to 1813 are articles by William Gamage, Jr., concerning uterine disorders in which he secured good results, probably in part because of alleviating anemia, by relatively large doses of iron. The history of Blaud's pills has been portrayed by Fitz, and as he has recorded, although Blaud used relatively large doses the amount of iron in his pills became reduced as decades passed by, but the number of pills advised remained the same. Then gradually after about 1900 the doses of iron advised became smaller, until within the past twelve years or so the value of relatively large doses was appreciated once more.

THE CHAIRMAN: I should like to ask Dr. Dameshek one question in regard to the pernicious anemia of pregnancy, and that is, if in any of his cases he had to terminate pregnancy.

DR. DAMESHEK: I wish to thank Dr. Heath and Dr. Minot for their excellent discussions of the paper. The many additional points I could have brought out but for lack of time will be adequately covered in the paper when published. The curious swings in the medical pendulum, particularly that one relating to the dosage of iron, are very interesting from the historical standpoint.

In answer to Dr. Chapin's question, pregnancy was terminated in one instance, but without effect upon the anemia. The enormous dosage of liver extract which must be given in these cases is indeed striking, and makes one suspect a lack of ability to utilize liver extract.

THE CHAIRMAN: The nominating committee reports the following for officers during the next year: for chairman, Dr. William H. Robey, Boston; for secretary, Dr. Clark W. Heath, Boston.

It was voted that the secretary be empowered to cast one ballot for these nominations, and these officers were elected.

THE CHAIRMAN: The next paper, on "Suction-Pressure Therapy in Peripheral Vascular Disease," will be given by Dr. E. Everett O'Neil.

SUCTION—PRESSURE THERAPY IN PERIPHERAL VASCULAR DISEASE

E. EVERETT O'NEIL, M.D.*

BOSTON

THE application of the principle of alternating suction and pressure in the treatment of chronic obliterative arterial disease is so well known that a repetition of its historical background and a discussion of the mechanical procedures involved seem unnecessary. We shall therefore confine ourselves to evaluating its efficiency as an agent in the production of collateral blood supply. This report is based on a series of 80 cases of occlusive arterial disease of different types. No attempt will be made to compare this method with others.

All the cases in this series have been put on a regular vascular regime; in brief, instructions as to the care of the extremities, cessation of smoking, increase of fluid intake, and so on. In addition, all have been instructed in the use of Buerger's exercises. Any cases showing trophic lesions were treated by the usual topical applications. Sixty of the 80 cases have been hospitalized for from four days to four weeks. The remaining cases have shown milder grades of obliteration and have been treated as ambulatory patients.

The suction-pressure machines used in this study have been of the conventional type manufactured by one of the leading equipment houses, and have employed both the Landis and the Hermann curves in their application. We have noticed no essential difference from the application of either method, insofar as end results are concerned. The pressures used have varied between 80 and 100 mm. of negative pressure and 10 and 20 mm. of positive pressure.

There were 33 cases of arteriosclerosis in this group of vascular diseases (Table 1). The ages ranged from thirty-nine to eighty, and showed a preponderance of males. Calcification of arteries

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From the peripheral vascular clinics of the Boston City Hospital and the Faulkner Hospital.

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was demonstrable by x-ray in 28 cases. There were 20 cases of thromboangiitis obliterans with age limits of twenty-seven to sixty, all males, and only 4 showing evidence of calcified vessels. In the group of 14 cases of arteriosclerosis complicated with diabetes the ages ranged from thirty-eight to seventy, the males dominated slightly, and 13 showed degenerative changes in the arteries. There

TABLE 1. *Summary of Cases.*

DISEASE	NO. OF CASES	AGE	SEX		CALCIFICATION OF ARTERIES
			Male	*Female*	
Arteriosclerosis	33	39-80	21	12	28
Thromboangiitis obliterans	20	27-60	20	0	4
Arteriosclerosis with diabetes	14	38-70	8	6	13
Peripheral embolism	7	24-56	7	0	—
Frozen feet	6	40-72	2	4	—

were 7 cases of peripheral embolism between twenty-four and fifty-six; there were 6 cases of frozen feet, all in males between forty and seventy-two.

Calcification of the arteries has been listed in this table for purposes of comparison between the arteriosclerotic diabetics and the cases of thromboangiitis obliterans and uncomplicated peripheral arteriosclerosis. In the former group 13 out of 14 cases showed radiologic evidence of calcification — a much higher percentage relation than either of the latter two groups. Clinically, it was observed in this group that there was a closer relation of calcification of arteries to symptoms than in either

TABLE 2. *Influence of Suction-Pressure Therapy on Prominent Signs and Symptoms.*

DISEASE	INTERMITTENT CLAUDICATION		ISCHEMIC PAIN		TROPHIC CHANGES	
	Improved	*Unimproved*	*Improved*	*Unimproved*	*Improved*	*Unimproved*
Arteriosclerosis	23	10	18	5	6	5
Thromboangiitis obliterans	10	6	19	1	2	6
Arteriosclerosis with diabetes	8	6	5	4	1	10

of the other two groups. In fact, it is not uncommon to find in routine clinical study extensive arterial calcification without accompanying arterial insufficiency, but in the diabetic the presence of calcified arteries is an ominous prognostic sign.

The influence of suction-pressure therapy on some of the outstanding signs and symptoms of chronic organic arterial disease has been of considerable interest to us. This method has no effect whatsoever on a part in which gangrenous changes have already set in. It has been reported elsewhere that gangrene seems to be limited as a result of treatment, and thereby a lower level of amputation seems permitted. This has not been our experience.

INTERMITTENT CLAUDICATION

We have noted a decidedly favorable effect in many cases of intermittent claudication (Table 2). Walking distance has been definitely increased. While we have no accurate method of measuring this increase, an approximate measurement could be obtained by having the patient accurately record the number of paces he could take before claudication occurred. After an interval of suction-pressure therapy he is then able to make a good comparison of his walking distance. In 23 cases of arteriosclerosis there was improvement of intermittent claudication; in 10 cases, no improvement. The latter were in the higher age brackets, where there was presumably arteriosclerotic involvement of the entire arterial tree. Improvement was noted in 10 cases of thromboangiitis obliterans; no improvement in 6. In the arteriosclerotic-diabetic group, favorable effects on intermittent claudication were observed in 8 cases, unfavorable effects in 6.

ISCHEMIC PAIN

The most striking effects of suction-pressure therapy come in that group of occlusive vascular cases in which ischemic neuritis is a prominent symptom. This is the type of pain usually found in the toes and feet where obliteration of the arteries has been going on for some time, which may precede or accompany trophic lesions, and which is often referred to as "rest pain." It is observed most frequently in thromboangiitis obliterans, and has always been one of the most intractable symptoms to treat. The interpretation of rest pain is somewhat difficult; it is probably due either to a piling up of connective tissue about the nerve adjacent to the blood vessels, or to a true anoxemia of the nerve itself. This ischemic pain responds very well, in the majority of cases, almost from the beginning of the suction-pressure treatment. In many cases relief of pain is permanent. In others, pain returns when the leg is removed from the boot, to be relieved when the leg again undergoes treatment. In Table 2, only those cases are listed as improved which seemed to get permanent relief of their pain. The others, we feel, are better submitted to some other therapy, for example nerve-crushing. In the arteriosclerotic group 18 cases showed improvement; 5 were unimproved. In 20 cases of thromboangiitis obliterans 19 were relieved; 1 showed no change. In 9 cases from the group of diabetics with arteriosclerosis, 5 were helped and 4 unaided.

TROPHIC CHANGES

In our experience, once trophic disturbances have taken place in the presence of vascular occlusions, suction-pressure therapy not only does not offer much in the way of improvement of healing, but may be a very dangerous weapon in promoting the spread of infection. If it is to be used, we urge the necessity of applying it only to those cases

which show clean wounds. This does not mean wounds that are bacteriologically sterile, but those which clearly show no gross sepsis. As shown in Table 2, 6 cases of arteriosclerosis having indolent ulcers were healed after suction-pressure therapy; 5 were only slightly affected or not improved at all. In the thromboangiitis obliterans group only 2 trophic lesions were aided as against 6 which showed no change, and this despite the fact that the associated pain was relieved in all 8. The poorest results occurred in the diabetic group, where only 1 ulceration seemed to be favorably acted upon. In 10 cases there was either no change or a tendency for the lesion to become worse. This is accounted for by two factors: first, the ulceration is usually infected; secondly, suction-pressure cannot be applied for long enough periods to do any good, for fear of producing an ascending infection.

EFFECT ON SKIN TEMPERATURES

The best index of improvement in the collateral blood supply of a limb is the improvement in the skin temperature. This has been recorded in these cases by the Tycos dermatherm. In a general way, the skin temperatures in most cases of obliterative arterial disease follow a similar pattern, increasing while the limb is in the boot and gradually declining after treatment, returning to the previous level in from twelve to twenty-four hours. The highest skin temperatures are noted in the thromboangiitis group; this is probably accounted for by the removal of the spastic factor through increased heat. All cases of thromboangiitis in this report have had skin temperature recordings under controlled room temperatures, and before and after spinal anesthesia. Many of these cases have not shown a temperature rise sufficient to justify sympathectomy, the increases ranging from 1 to 4°C. After these cases have submitted to reasonably long intervals in the suction-pressure chamber, there is a temperature rise corresponding approximately to the level observed after spinal anesthesia. And, as may be evident, the higher the temperature increase the greater the amelioration of symptoms.

TABLE 3. *Average Duration of Treatment and Average Increase of Skin Temperature Following Treatment.*

DISEASE	AVERAGE DURATION OF TREATMENT	AVERAGE INCREASE OF SKIN TEMPERATURE
Arteriosclerosis	37 hours in 19 days (longest, 110 hr. in 58 da.)	2.8°C.
Thromboangiitis obliterans	42 hours in 24 days (longest, 365 hr. in 409 da.)	4.6°C.
Arteriosclerosis with diabetes	22 hours in 20 days (longest, 42 hr. in 10 da.)	1.6°C.
Peripheral embolism	20 hours in 4 days	Not recorded
Frozen feet	18 hours in 8 days	Not recorded

The average skin temperature increase in 10 cases from the arteriosclerotic group, ten hours after treatment had ceased, was 2.8°C. (Table 3 and Chart 1). The duration of suction-pressure therapy in this group was thirty-seven hours in nineteen days, the longest application to any individual case being one hundred and ten hours in fifty-eight days. In 10 cases of thromboangiitis obliterans the average temperature rise was 4.6°C. The average length of treatment was forty-two hours in twenty-four days, the longest individual treatment being three hundred and sixty-five hours in four hundred and nine days.

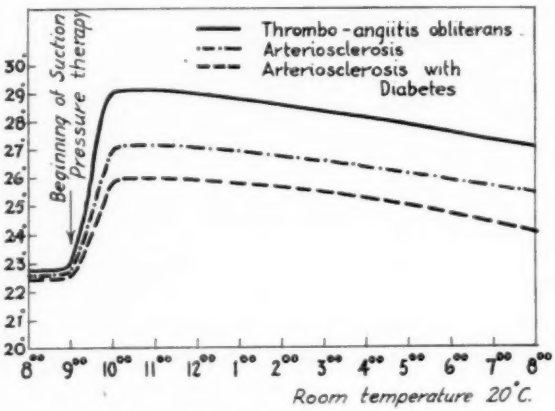

Chart 1. *Average rises in skin temperature following suction-pressure therapy.*

It is perhaps important at this point to consider this last case in detail, as an example of what can be done with long-continued suction-pressure treatment in controlled and selected cases.

A Jewish tailor of 55 entered the Faulkner Hospital in March, 1936, complaining of intermittent claudication in both legs, with a walking distance of one block, and pain, coldness and discoloration of the left great toe. This pain had been increasing in intensity for the past 2 months, was worse at night when the patient was resting, and responded only temporarily to narcotics. The patient smoked two packages (plus) of cigarettes daily, had been forced to give up his work, and got around with the aid of crutches. Examination revealed absence of pedal pulses in both feet, absent popliteal pulsation on the left, a weak popliteal pulsation on the right; there was good femoral pulsation on both sides. The left great toe was cold, and showed a purplish mottling in the distal two thirds. On elevation of the legs there was a marked waxy pallor, with a resumption of a moderate peripheral rubor of the feet when they were lowered. Roentgenologic examination showed no calcification of the arteries. Skin temperature readings before and after the Landis test and spinal anesthesia showed an elevation of only 4.4°C. A diagnosis of thromboangiitis obliterans was made.

The patient was hospitalized for 2 weeks, during which time he was put on a circulatory regime which included the prohibition of tobacco, care of the extremities and postural exercises. He was given 3 hours of suction-pressure therapy daily. When discharged his rest pain had completely disappeared. The claudication had improved slightly. The toe was still discolored but warmer. Since discharge from the hospital the patient has received 6 hours' treatment on 3 days a week. At the present time, 1 year later, after 365 hours of treatment in 409 days, he has no intermittent claudication. He can walk a mile

without distress. He has no rest pain. His toe has returned to a normal pink color. Skin temperature readings show a sustained increase at a level of 4.5°C. (Chart 2).

In the arteriosclerotic-diabetic group, the average rise in 10 cases was 1.6°C., and the average length of treatment twenty-two hours in twenty days; the longest individual case was forty-two hours in ten days. In the acute vascular occlusions, represented

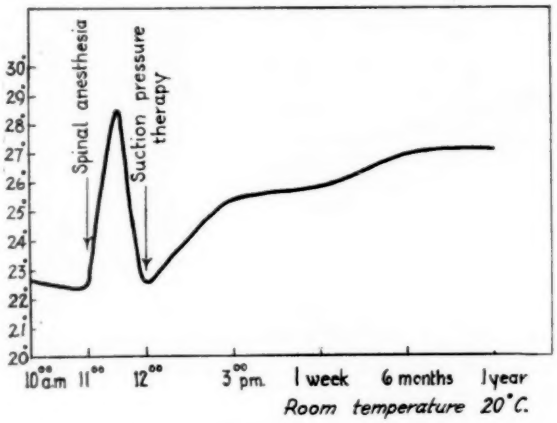

Chart 2. *Skin temperatures in a case of thromboangiitis obliterans that received prolonged treatment.*

by frozen feet and peripheral embolisms, suction-pressure therapy is necessarily given in more concentrated form, since the time element here is an important factor. In 7 cases of occlusion of the peripheral arteries, twenty hours of suction pressure were applied in four days. In 6 cases of frozen feet, eighteen hours of treatment were given in eight days.

RESULTS

The only criterion of success in the treatment of peripheral vascular occlusions is the return to normal function of the part involved. Anything short of this cannot be considered a good result. This return, as we have suggested above, will be manifested by the absence of pain, lengthening of walking distance, healing of trophic lesions and increase in vasodilatation. In Table 4 are listed the number of cases meeting these requirements. Out of a total of 33 arteriosclerotics, results were good in 18, fair in 6, poor in 9. Cases listed as fair showed moderate improvement in their condition, but enough circulatory insufficiency remained after treatment to prevent them from resuming previous occupation or activity. Cases listed as poor had recourse to other treatment, had thigh amputations, or died. In a series of 20 cases of thromboangiitis obliterans, 10 obtained good results, 2 fair, and 8 failed to respond to treatment. In the group of arteriosclerotics complicated by diabetes, there were 4 good, 2 fair and 8 poor results out of a total of 14 cases.

TABLE 4. *Summary of Results.*

DISEASE	NO. OF CASES	RESULT		
		Good	*Fair*	*Poor*
Arteriosclerosis	33	18	6	9
Thromboangiitis obliterans	20	10	2	8
Arteriosclerosis with diabetes	14	4	2	8
Peripheral embolism	7	4	—	3
Frozen feet	6	5	—	1

The results in the peripheral embolism group also need some explanation. From a total of 7 cases, 4 are listed as good, 3 as poor. It is the experience of any surgeon who has done embolectomies that the time element is the important factor in success or failure. There is little likelihood of a satisfactory outcome if an embolectomy is done after four hours. It has been our experience that no more can be expected from suction-pressure therapy than from embolectomy. Early recognition and treatment are essential to success no matter what therapeutic method is pursued. Since alternating suction-pressure is the less distressing to the patient, we believe that it will replace operative procedures in these acute occlusions. However, where the embolus is easily accessible, as at the bifurcation of the femoral, popliteal or brachial arteries, a simple embolectomy followed by suction-pressure treatment may be the procedure of choice. All the failures in this group have resulted because of late application of treatment, after gangrene had definitely set in.

Striking results were obtained in the group of frozen feet, where out of a total of 6 cases 5 were good and only 1 was poor. The explanation of this may lie in the fact that at the first observation of frozen extremities it is difficult to tell the depth of involvement. Many of these cases, with marked gangrenous changes in the outer layers of skin, get better without any treatment, and one might therefore easily ascribe virtues to a treatment which need not have been applied. One cannot help, however, being impressed by the very rapid return to normal of frostbitten extremities after an interval of suction-pressure therapy.

CONTRAINDICATIONS

In the beginning, suction-pressure therapy was perhaps injudiciously applied in many cases, with resulting complications, and in certain instances fatalities. Further experience has taught us to avoid many of these pitfalls. For example, suction-pressure therapy should never be used in the presence of infection, whether it be associated with an open ulceration or take the form of an early cellulitis or lymphangitis. The main cause of failure in the cases of arteriosclerosis associated with diabetes is due to the tendency of this group to show a rapidly ascending sepsis following the breaking down of skin lesions. Again, one has to use extreme caution in applying the negative-positive pressures in the acute phases of thromboangiitis obliterans.

Many of these cases may show a migrating phlebitis which will of course interdict the use of the chamber; but not a few have a low-grade phlebitis, not apparent, which may flare up within a very short time after this therapy is started. It is very questionable also whether suction-pressure treatment is of any value in advanced arteriosclerosis of the extremities. These cases show involvement not only of the main arterial pathways, but also of the smaller arterioles on which we depend for improvement of our collateral vascular supply. If after a reasonable length of treatment (thirty to forty hours) no improvement is visible, the chances are against further therapy being of any value. We are loath to admit that many of these advanced cases of arteriosclerosis represent terminal disease, and that many of them do better with artificial limbs. Too often have we seen attempts to save an extremity, in which the vascular condition was so poor as to render the chances of success hopeless from the outset, result in a catastrophe which might well have been averted by an early amputation.

SUMMARY AND CONCLUSIONS

Eighty cases of occlusion of the peripheral arteries treated by alternating suction and pressure have been reviewed.

The best results were obtained in the acute occlusions, when treatment was instituted before tissue changes had progressed too far.

The poorest results were observed in arteriosclerosis of the extremities where diabetes was a complicating factor, and particularly where calcification of the arteries was shown by x-ray, denoting a low collateral potential.

Negative-positive pressure treatment is of definite value in the early and moderately advanced cases of peripheral arteriosclerosis and thromboangiitis obliterans, exerting a marked beneficial influence on intermittent claudication and ischemic pain in these cases. Its value in the later stages is doubtful.

In all types of chronic peripheral obliterative diseases to which suction-pressure therapy may be applied, it must be stressed that long periods of treatment are necessary for success. Since the tendency of any occlusive disease is to progress, it is important to keep ahead of it, by frequent and continued applications of treatment.

In conclusion, it must be obvious that while suction-pressure therapy is not a panacea for all circulatory ailments of the extremities, it is nevertheless a distinct addition to the various therapeutic measures already at our disposal, and should be evaluated in relation to the demands of the individual case.

270 Commonwealth Avenue.

DISCUSSION

THE CHAIRMAN: The discussion will be opened by Dr. Allen S. Johnson, who will approach the subject from the medical standpoint.

DR. ALLEN S. JOHNSON, Springfield: Before we select one of the various methods designed to increase a limb's vascularity we must determine the nature and extent of the interference with the peripheral circulation. It is unfortunate that the research use of costly and relatively complex instruments like the thermocouple and the oscillometer has given to many the impression that the diagnosis of peripheral vascular disease is within the grasp of only a chosen few. Every practicing physician with only bedside equipment has at his disposal at least half a dozen useful methods for diagnosing this condition if he will but use them. And use them he must if he is to recognize early impairment of the peripheral circulation while it is yet amenable to treatment.

Although the pulsation of an artery is an imperfect guide to follow, peripheral pulses in the limbs should be palpated, if only to compare the amplitude of pulsation in symmetrical parts. Pulselessness is the chief sign of a proximal obstruction in the artery displaying it, and a diseased artery often presents a smaller pulsation than does a normal one. But in comparing symmetrical pulsations the two limbs should be rendered equal in temperature, as a cold limb has a smaller pulse than a warm one, even in normal subjects. Furthermore, the limb should be examined in the warm state before concluding that pulsation is absent. A film of oil between the artery and the palpating finger may render faint pulsations more easily perceptible.

The blood-pressure cuff is applied to the arms of arteriosclerotic patients with solemn regularity, but it is seldom used to compare the head of pressure in the two lower extremities. Pressure measurements may be taken above the knee and above the ankle by either the palpatory or auscultatory method, and while not so satisfactory as oscillometer readings they are of considerable significance.

A limb with impaired circulation develops pallor on elevation, which can be accentuated by rapid plantar and dorsal flexion, and rubor on dependency. Here again the limb should be warm when tested.

Whereas skin temperature is best measured with special instruments such as the electric or mercury skin thermometer, the information gained by palpation may be of considerable value. Sir Thomas Lewis recommends the dorsal surface of the middle phalanx of the flexed finger as the best testing surface, but it must itself be warm. Such observations will quickly determine marked differences in temperature, and therefore in blood supply, between symmetrical areas on the two extremities. If a simple comparison of this sort fails to reveal thermal discrepancies when the circulation to one limb is suspected of being deficient, the two limbs may be simultaneously exposed to cooling by removal of the bedclothes, or warmed by simultaneous immersion in water and then exposed to cooling after thorough drying. The limb with the impaired circulation will warm more slowly and cool more quickly. More detailed studies of a similar nature are given in Lewis's* book *Vascular Disorders of the Limbs* and in a paper by Landis and Gibbon.†

The procedures so far described require only the equipment ordinarily carried in the practitioner's bag. If this be supplemented with a sterile needle and an ampule of

*Lewis, T.: Vascular Disorders of the Limbs. P. 14. New York: The Macmillan Co., 1936.

†Landis, E. M., and Gibbon, J. H.: A simple method of producing vasodilatation in the lower extremities. Arch. Int. Med. 52:785, 1933.

histamine, the cutaneous histamine reaction may likewise be performed as a bedside observation. One tenth of a cubic centimeter of the 1:1000 solution may be injected intradermally or applied as the allergist performs a scratch test. Normally a wheal with a surrounding zone of hyperemia is produced in from three to five minutes. This reaction is absent when the head of pressure in the skin vessels is insufficient to fill the capillaries dilated by the histamine. In patients with frank gangrene the lowest level of safe amputation can thereby be determined; and during a course of treatment with drugs or physical measures the improvement of the collateral circulation can be visualized.

THE CHAIRMAN: The next paper is entitled "The Wisdom of the Human Body." It is with real affection that I introduce the speaker—an inspiring teacher, a distinguished citizen, a pioneer in medical social service. We honor ourselves in welcoming Dr. Richard C. Cabot.

THE WISDOM OF THE HUMAN BODY

RICHARD C. CABOT, M.D.*

CAMBRIDGE

I DO not know whether this section of the Massachusetts Medical Society will be interested in the ideas which I have been asked to speak of here today. They are ideas that have interested me. I agree with the idea which has been expressed so beautifully in the title of Dr. Walter B. Cannon's book, *The Wisdom of the Body*. That title was given to Dr. Cannon by Professor Starling in 1923. I had previously been talking for some years on a subject which I called "The Intelligence of the Body." Then Dr. Cannon came out with this wonderful book, and I saw at once the strength both of his work and of his title.

A considerable period of residence on the surface of this earth has not impressed me with the wisdom of the human mind. It is the wisdom expressed through the human body that has impressed me. I saw it in the experiences of my teaching work. I have seen many autopsies at the Massachusetts General Hospital, and there had occasion to see things that I never expected to see.

I suppose anyone who thinks of an autopsy thinks of something that may be of interest but that can hardly be a matter of inspiration. It can hardly help being something discouraging, because it shows how disease has conquered a man. But the surprising thing to me, as I have had the opportunity to see about five thousand autopsies, was the inspiration that has come to me through seeing in them the wisdom not of the human mind but of the human body. I am going to speak of a few facts well known, not a single thing new to you in any way; the only possibility of interest is in the interpretation which I propose to give to these perfectly familiar facts.

I shall speak of the wisdom of the body, then, under four headings: reserve, as in the sense of a bank reserve; balance; compensation; and defense.

Presented at the annual meeting of the Massachusetts Medical Society, Boston, June 1, 1937.

*Professor of clinical medicine emeritus, Harvard Medical School.

RESERVE

I suppose you have sometimes wondered, as I have, why we have to have so many feet of intestines. There are all sorts of physiologic reasons, of course, but one of them undoubtedly is that something may happen to any one of us any day whereby a skillful surgeon may have to take out four or five feet of our intestines. We are just as well off without it because we have such an ample reserve.

The reserves stored in the lungs struck me particularly thirty years ago. I had the honor to know Dr. Trudeau. He became pretty lonely sometimes up there in the cold winters at Saranac. I visited him occasionally, and he frequently asked me to examine his lungs. It amused him. I got used to the fact that over one lung I could hear no breath sounds whatever, and so had reason to believe that it was nearly functionless. There was very little to hear over the upper half of the other one. Yet he was able not only to get on but to excel. Why, you should have seen the way he would go! Twice as much alive as you or I! He was the king of men, not only in medicine, but in doing whatever there was to be done in that district. He had so much reserve in his lungs that he could do twice as much with half of one lung as you or I could do with two!

When I first began to see operations as a young man, I wondered at the number of vessels that were cut on the way in. They would cut the vessels, snap them, and leave them to be tied later. I wondered what became of all the blood that went through the veins which the surgeon had cut. How could the patient stand it? Because he had such an extraordinary reserve of small veins, so that in his struggle for existence he could lose a good many and still get along well enough.

BALANCE

A combination of balances constitutes our health. You know the word which Dr. Cannon uses all

through this book, the word "homeostasis," which means keeping the same, or balance. He has perfectly expressed in that word what we all knew less clearly before, that our health is a matter of balances — the balance of temperatures, of various chemical elements entering and leaving the body, of water and of the total reaction of the body.

We have been seeing this afternoon some of the disturbances of our heat balance brought about for therapeutic purposes by heat treatment. But nature knew all along that to produce fever was one of the ways of curing disease. Nature has always used thermotherapy. A few years ago physicians tried to reduce fever temperatures. Now we produce them, as we have heard this afternoon.

Take the acid-alkali balance. Of course, you all know that the body has to be kept very close to neutral, and does in fact stay there. That seems natural enough, until we remember that almost everything we do drives our bodies to one side of neutral or to the other. If you ran round this room fast, your body would go over to the acid side. If you eat a big meal with many green vegetables, you are pushed to the alkali side. Our balance in the relation of acid to alkali — how could it be kept if it were not for the production, now of acids, now of alkalies, in the body?

I once asked a chemist to give me a figure of speech to show how closely our acid-alkali balance has to be kept if we are to live. You may remember at Chicago during the World's Fair there was a thermometer one hundred feet high. This physical chemist told me that the human body compared to that thermometer could not stand the rise and fall of more than *three inches* in one hundred feet (representing balance of acid and alkali) without death.

COMPENSATION

Compensation is one of the most familiar of facts to doctors. One of the most outstanding examples of compensation I ever saw was at the Canton Hospital for Crippled Children. Dr. Fish showed us a little boy with infantile paralysis who could not use his legs at all, but had learned to walk on his hands instead. He was happy and proud about it and would show off, walking on his hands and with his legs folded up behind his head. He walked on his hands down the hall and up the platform. By work hypertrophy his arms had grown enormously. They were twice as big as ordinary boys' arms, and I saw him later sitting in the pitcher's box of the school's baseball field and pitching a very swift curved ball.

I always remember the case of Dr. James M. Mumford. He contracted rheumatic heart disease when he was seventeen. He died at fifty-four, I believe of strangulated hernia. All that time he practiced medicine very actively, taught surgery, carried on a sanatorium, and all that with a mitral valve that would just admit the blades of a pair of scissors shut up. Compensation had made his heart nearly thrice the normal size so that it carried him well through an active life. You know, of course, how often a person suffers injury to his kidney in an automobile accident. As the wheel passes over the body the twelfth rib cuts into the kidney, and the kidney is so damaged that it has to be removed. It is perfectly safe for the surgeon to remove it because the other kidney is sure to double its size by compensatory hypertrophy. We do not always stop to think what happens when the kidney duplicates its size. It is as complicated a machine as an automobile. Think of the wisdom of the body that can duplicate at need the machinery of the remaining kidney so that one can get along just as well with a single kidney as he did before with two!

DEFENSE

If you sprain your wrist, the wisdom of the body wants to put on a splint, so it makes your wrist stiff and sore and swollen. It has an internal splint before the surgeon puts on the external one. The wisdom of the body defends us by throwing out poisons, by vomiting, by diarrhea, by the breath, for instance by the alcoholic breath that even the policemen can smell. All these methods of throwing out poisons are familiar to us.

Antitoxin, which we think of as manufactured outside the body, the body itself manufactures. Long before we had diphtheria antitoxin the body manufactured enough of it inside the body to result in cure in 60 per cent of the cases, and so with the other infectious diseases. Typhoid fever, over which we have no therapeutic control whatever, used to discourage us; it was said that we had 10 per cent mortality. We were not proud that we had a 90 per cent cure by the body's defense mechanisms.

Recall what the leukocytes do in the way of warding off infection! Every time you get a splinter in your finger you might have blood poisoning if it were not for leukocytes that come rushing to your aid and build with their bodies a wall between the attacking bacteria and the blood stream. In an appendix operation, think of the millions and millions of leukocytes organized around the appendix to wall it off and so to defend the peritoneum. Young men, such as I see before me, cannot realize as I do the former feats of the body in surgery. I wonder if anyone here has ever seen an appendix extracted through the abdominal wall by the wisdom of the body, without surgery. I have. You have all seen, I suppose,

an appendix abscess evacuated through the rectum by the surgery slowly but efficiently done by the healing powers of the body.

I can sum all this up by describing one case. I once saw an autopsy on a man killed by an automobile. He was brought into the hospital almost dead. He was sixty-five years old and had never been sick. He had never called a doctor. He had never used medicine. He had always been perfectly well. His wife came with him and told us these things. I was at the autopsy. We found four fatal diseases. And the man in perfect health! That hit me between the eyes.

What were these four diseases? The man had *pulmonary tuberculosis.* We felt something hard at the top of one pulmonary apex. The knife-edge was broken on a stone in the lung — lime salts — walling off a focus of tuberculosis so that it was harmless. We found *arteriosclerosis,* with high blood pressure, I suppose, and with a big heart which had compensated for that. He had a considerable degree of *chronic nephritis,* but there was enough sound kidney left to carry on satisfactorily. He also had *cirrhosis of the liver.* He was a bartender and not a total abstainer. But he still had liver substance enough to do the liver's chemical work, and the vascular work of carrying the intestinal blood back to the heart was done by a new set of blood vessels running over and under the liver and so carrying the blood around it and back to the heart. So much for the facts. Now for their interpretation.

These things are made possible by the wisdom of the human body. This man had four fatal yet perfectly harmless diseases. He was a well man until he was killed by an automobile! We say that this is done by the healing power of nature. But what is nature? It is an imaginary entity, a superstition, one of those generalities like liberty, fraternity, equality. You see statues of them in Paris. You know there is no such thing. What are the characteristics of this power? The first is that it has superhuman wisdom. We all admit the wisdom of the healing powers at work in the body, powers which our therapeutics are a very long distance behind. Secondly, the power is extraordinarily biased in favor of life as against death. There is an old story of the man finding a bear after him. He was not a religious man, but he prayed. He prayed the Lord not to favor either him or the bear but just to be perfectly neutral. "And then," he said, "You will see the greatest fight You ever saw in Your life."

Now the point I am making is this. Here is a power that is *not* neutral, but tremendously biased on the side of life as against death. It does not win every time, and it still leaves plenty of work for all us doctors to do; but still it does about ten times as much as all that we can do to keep life from being overcome by death. We see, then, a force that has superhuman wisdom and that cares tremendously about life. It is always on the job, and does not make half so many wrong diagnoses as I used to make, and perhaps some others in this room.

Where does this force come from? Where do we get the healing substances in our tissues? Out of our food and water and the air we breathe, that is, out of the bounty of the universe. We cannot make food, air or water. We find the air and the water; we cultivate our food which comes out of the cosmos which has created us and gives us the life that brought us here today. Now, if we see in our medical work a power superhuman in wisdom and in goodness, one that works all the time and that comes out of the cosmos, I do not see why we should not call it by its natural name. I do not see why we should be afraid of that name. It is perfectly obvious that it is God. Why should we physicians be afraid to use those letters, G-O-D? That is the only proper word that represents those facts; "nature" is a very foolish word to use for them, for no one knows what that word means. So instead of "vis medicatrix naturae" we should say "vis medicatrix Dei." It is the power of God on which each one depends today for the fact that he is here instead of being underneath the earth.

But, you may say, this power that creates and maintains us also creates and maintains the bacteria which would destroy us. Yes. The question is, Can they and we learn to live and let live? Can we learn to live with men, with inanimate things like fire and floods, and with animal and insect pests, and finally, can we learn to live with bacteria? We have to learn to get along with them on penalty of being wiped out. The positive law of life is: live and learn, because if we do not learn we cannot live. The negative law of life is: do not overrun others or be overrun by them. They are still working overtime on the Ohio and the Mississippi because men have stubbornly refused to learn how to live peacefully and helpfully with the forces of nature. Men are stubborn, and so they are always thinking of war. Bacteria are stubborn, and so we must be always thinking of disease. We are stubborn and stupid in not getting over the idea that overrunning or being overrun are perfectly natural things.

If we can learn to live ourselves, to let others live, to accommodate ourselves to them and to limit them so that they cannot overrun us, we can get along well. Otherwise we cannot.

What has this idea of the healing power of God to do with the practice of medicine? I say, use

the idea. Use it and so help yourself and your patient! It means that when you start treating a patient, you know, and your patient will be glad to know, that you have a tremendous force on your side. Let the patient know it. I think it would make our treatment more effective. I believe we should add to our confidence and the patient's confidence, which is one of the greatest things that our patients need, in organic as well as functional diseases. Anybody would have more confidence in his own life and in others' lives if he admitted the potency of this tremendous force.

There is no reason, then, so far as I see, why doctors should be afraid of the simple, old-fashioned word, God. The medical profession has learned in studying disease more about the meaning of this word than the vast majority of the so-called religious people. Why not tell this truth, because it is true?

101 Brattle Street.

DISCUSSION

THE CHAIRMAN: This splendid address can hardly be discussed, but Dr. Pratt will, I know, say some words of appreciation.

DR. JOSEPH H. PRATT, Boston: I gladly acceded to the request of the officers of this section that I should join them in paying a tribute to Dr. Richard C. Cabot, a name we are proud to have on the rolls of the Massachusetts Medical Society. We are all delighted to have him with us today.

At a time when many liberal theologians have lost their belief in God and in place of theism have proclaimed a religion without God, namely humanism, it is heartening to hear Dr. Cabot present an argument for a wise and good Creator based on the "wisdom of the body." Dean Matthews, of St. Paul's, London, states in his recent book, *The Purpose of God,* that "of all the reasons which have been alleged for belief in God, the argument from design, called by the learned the 'teleological argument,' has always made the most direct appeal to the masses of mankind." That Dr. Cabot's views on this subject are in accord with those of leaders of modern theological thought is indicated by Dean Matthews's statement that "the time is plainly ripe for a reconsideration of traditional 'proofs' of Theism, for the reign of Kant is coming to an end." It has always had the support of common sense. Roman Catholic thinkers have never bowed the knee to Kant, and have always adhered to the conviction that belief in God is based on reason.

This is, so far as I know, the first contribution to theology presented at a meeting of the Massachusetts Medical Society. My old teacher, Professor Krehl, of Heidelberg, had the degree of Doctor of Theology conferred upon him a few years ago. It seems to me that no member of the medical profession in America is worthier of such an honor than Dr. Cabot.

When I was a young man studying in Germany, the leaders of medicine whom I interviewed would always ask, when the name of an American physician was mentioned, one question. This was not "What position does he hold?" but "What has he done?" If this inquiry were made regarding Dr. Cabot, it would be an easy question to answer because he has done so much. He graduated forty-five years ago from the Harvard Medical School. After he finished his internship in the Massachusetts General Hospital there was no place for him on the staff of the hospital. In the medical outpatient department there were many patients and a small staff, but no attempt was made to increase it. In those days only the attending physician and an intern examined and treated the patients in the male and female medical clinics. The long period of six years elapsed after his graduation before he was appointed to the staff.

He began his life's work during a period of medical inertia in Boston, but he created opportunities for himself. While an intern he began to make blood examinations. That was a new thing in Boston. I believe he got his inspiration from Dr. William S. Thayer, of Baltimore, who brought back from Germany Ehrlich's technic for staining blood films. Dr. Cabot learned the methods and read the German literature. He stimulated and taught the interns who came after him, with the result that the Massachusetts General Hospital was one of the first hospitals in the world in which study of the blood was part of the routine examination. In 1896 he published the first book in English on hematology. In the preface he stated that in the previous three years three thousand blood examinations had been made in the hospital, chiefly by the interns, and that he himself had done over a thousand. His *Clinical Examination of the Blood* ran through five editions in eight years.

In 1905 he organized hospital social service. He has lived to see it spread over the world. It is recognized today that no hospital for the poor can do its work properly without an efficient social service department.

In the same year he secured the support of Dr. Osler in forming the Interurban Clinical Club. This society was organized to bring together twice a year a small group of young teachers connected with the medical schools of the East with the object of gaining fresh knowledge from each other through demonstrations and informal clinics. This society is still an active force in medical education, and similar ones have been formed in other parts of the country.

Dr. Cabot introduced the case method, so successful at the Harvard Law School, into the teaching of clinical medicine, and published a book which enabled teachers in other schools to utilize the cases he had found instructive. This was followed by the establishment of the clinicopathological conference. This important American contribution to methods of medical education was made by Dr. Cabot. Today probably every well-organized teaching hospital in the country has its clinicopathological conference.

Convinced of the close relation that should exist between the work of the clergyman and the physician, he has been instrumental in securing the appointment of a chaplain at the Massachusetts General Hospital, who supplements the work of the physician by giving needed help to the personality of the patient. Dr. Cabot's latest book deals with the result of this joint work and was written in collaboration with Mr. Dick, the hospital chaplain. This simultaneous treatment of the soul and the body of the patient was called by Cotton Mather "the angelical conjunction."

THE CHAIRMAN: In adjourning, let us stand in honor of Dr. Cabot. The meeting is adjourned.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 23461

PRESENTATION OF CASE

First Admission. A fifty-two-year-old white mechanic was admitted complaining of abdominal pain and anuria of eighteen hours' duration.

For the past ten years he had been upset by fried or fatty foods. Three months before entry, following a meal which included roast pork, he was suddenly seized with excruciating right upper quadrant pain that radiated through to his back and up to the right shoulder blade. The attack subsided spontaneously in four days without treatment. He had no jaundice, clay-colored stools or other symptoms. On the evening before admission, about one hour after eating pork chops, he was seized with an exactly similar excruciating pain with the same radiation. His physician gave him three ¼ gr. doses of morphine during one hour, which failed to give real relief. The pain persisted throughout the night, but subsided somewhat in the morning. He had not voided since the onset of pain. He vomited once during the morning.

His past history and family history were noncontributory.

Physical examination revealed an extremely ill man lying in bed. He was restless and cried out with pain every time he moved. The abdomen was distended and showed board-like rigidity throughout, particularly in the upper part, with generalized tenderness, which was most acute in the midepigastrium. There was also acute costovertebral and flank tenderness, but no psoas spasm. A catheter was put into the bladder but no urine was obtained. The blood pressure was 108 systolic, 80 diastolic.

The temperature was 99°F., the pulse 70. The respirations were 20.

The blood showed a white cell count of 22,500. The nonprotein nitrogen of the blood serum was 58 mg. and the serum protein 4.8 gm. per cent. The CO_2 combining power was 58.3 vol. per cent. The chlorides were equivalent to 89 cc. of N/10 sodium chloride. The van den Bergh was normal, and a blood Hinton test was negative.

Soon after admission 1800 cc. of 5 per cent dextrose in saline was given and shortly after that he began to pass some urine which was negative on examination. An abdominal tap yielded 10 cc. of bloody fluid from which no organisms could be cultured. On the day following admission his blood pressure was very difficult to obtain, his pulse was very weak and his extremities became quite cold. His temperature rose to 101.5°F., where it remained for five days. He was considerably improved the following day although his nonprotein nitrogen had risen to 110 mg. per cent. His serum protein was 5.5 gm. per cent. He was given a transfusion of 500 cc. of blood. On the fifth day the blood pressure was 160 systolic, 100 diastolic, and the nonprotein nitrogen 60 mg. and the protein 5.1 gm. per cent. The chlorides were equivalent to 113 cc. of N/10 sodium chloride. His abdomen was still markedly distended, but there was some peristalsis. He was given another transfusion of 500 cc. on the next day, with about 5500 cc. of other fluids. The temperature fell to 100°F. for one day, but rose again to 103°F. on the following day and remained high for the next ten days. On the seventh day he began to develop edema of his back and flanks, and became mentally irrational. During the next two days the abdominal distention subsided to a considerable degree and peristalsis improved. The edematous area in the left flank became indurated and red, and on the thirteenth day it was incised. Very little free fluid was obtained but the tissues were riddled with areas of fat necrosis. Drains were inserted down to the tail of the pancreas. No organisms were obtained on culture. On the next day the nonprotein nitrogen was 50 mg., and the van den Bergh 4.69 mg. per cent direct. The chlorides were equivalent to 109 cc. of N/10 sodium chloride. The blood showed a white cell count of 20,700 and a red cell count of 4,520,000, with 82 per cent hemoglobin. During the next week he improved somewhat, with a slight fall in temperature. There was very little drainage from the left flank. He was able to take but little food by mouth. On the twenty-first day a jejunostomy was performed through which he was fed a high-vitamin, high-caloric diet. The flank incision had begun to discharge pus and necrotic tissue.

On the twenty-second day his nonprotein nitrogen was 24 mg. per cent. At that time a mass was palpable in the right epigastrium. He gradually improved, with a steady fall in temperature until his chart became flat on the thirty-third day. On the fortieth day he suddenly complained of severe pain in his epigastrium and had marked tenderness in his right upper quadrant. The pain subsided within thirty-six hours, but recurred again in milder form five days later. A fasting blood sugar taken at that time was 157 mg. per cent. On the fiftieth day the epigastric mass was palpable five fingers below the costal margin and was mod-

erately tender. The flank wound was gradually healing. In the previous five days he had gained 6 lb.; there was definite pitting edema of both ankles. The serum protein was 4.9 gm. and the nonprotein nitrogen 23 mg. per cent. The chlorides were equivalent to 108 cc. of N/10 sodium chloride. The CO_2 combining power was 65.8 vol. per cent, and the van den Bergh was normal indirect. During the next two weeks he improved rapidly, developed an excellent appetite and gained weight and strength. The mass in the right epigastrium was still palpable but non-tender. A sugar tolerance test showed a fasting sugar of 89 mg. per cent, 153 mg. at one half hour, 182 mg. at one and a half hours and 96 mg. at three hours. The van den Bergh two days before discharge was 3 mg. per cent direct. He was discharged on the sixty-sixth day.

Second Admission (two weeks later). Following discharge he noticed that his abdomen slowly increased in size and that he became mildly constipated. There was no blood in his stools and no change of color. His appetité remained good but eating caused him some distress. He also noticed moderate edema of his legs which subsided somewhat at night. He had no pain, vomiting or jaundice. On admission, examination revealed distention of the abdomen with shifting dulness in the flanks and a definite fluid wave. There was no edema of the extremities. The liver was not enlarged to percussion.

The fasting blood sugar was 88 mg., the nonprotein nitrogen 23 mg. and the serum protein 5.2 gm. per cent. The chlorides were equivalent to 101 cc. of N/10 sodium chloride. The CO_2 combining power was 64.3 vol. per cent, and the van den Bergh was normal. The Takata-Ara test was positive. The urine contained a very slight trace of albumin with 10 or 15 white cells per high-power field. The white cell count of the blood was 12,600, with 62 per cent polymorphonuclears; and the red cell count was 3,710,000, with 60 per cent hemoglobin.

An abdominal tap on the day of entry yielded 3200 cc. of clear brown fluid with a specific gravity of 1.012. X-rays on the third day showed no evidence of disease in the esophagus, stomach or duodenum. The kidneys were poorly outlined, and there was a moderate amount of gas and fecal material overlying them. The chest was essentially negative except for a high right diaphragm, a relative enlargement of the left ventricle and slight tortuosity of the aorta.

His condition remained essentially unchanged until the tenth day when he began to complain of colicky abdominal pain and showed generalized abdominal tenderness which gradually increased in severity. His white blood-cell count was 38,700. He was given two transfusions in the next two days. On the morning of the twelfth day he discovered that he was unable to move his legs, and they were found to be cold and blanched. A weak femoral pulse could be felt on the left, but none on the right. Both legs were put in glass boots without improvement. His temperature rose to 100°F., and he died.

Differential Diagnosis

Dr. Robert R. Linton: The first part of this story is one of gall-bladder disease complicated by one of two conditions. The first is the possibility of a ruptured gall bladder resulting from distention due to acute infection. In view of the lack of symptoms of an acute cholecystitis, I think this possibility is not likely. The other condition is acute pancreatitis.

On his admission he had the signs of a peritonitis. The marked collapse and the rigidity of his upper abdomen are consistent with acute pancreatitis. The normal temperature, pulse and respirations seem unusual in a man who was as sick as he was. The lack of temperature would suggest the hemorrhagic type of pancreatitis rather than an infectious pancreatitis. The laboratory data on entry showed a leukocytosis consistent with a peritonitis. The blood nonprotein nitrogen showed definite nitrogen retention and is directly associated with the fact that he was unable to pass his urine. I explain his anuria entirely on the fact that he was an extremely sick man, probably suffering from secondary shock as is indicated by the low blood pressure. It is not unusual to find a suppression of urine under such conditions. An abdominal paracentesis was done for diagnostic purposes and yielded bloody fluid. This suggests either strangulation of intestines or hemorrhagic pancreatitis.

The diagnosis of pancreatitis is of course substantiated by the description of the inflammatory mass in his left flank which showed areas of fat necrosis. It is not surprising that he drained very little at first and then subsequently drained a considerable amount including large pieces of necrotic tissue. This is a common sequence of events following the drainage of an acute pancreatitis. The necrotic tissue represented pieces of the pancreas itself. The mass that he developed in his epigastrium I think is of great importance in the ultimate diagnosis. It presents an interesting problem because according to the history it was present at one time and then disappeared.

The fact that he had a high blood sugar would indicate that perhaps his islands of Langerhans were temporarily interfered with, as his blood sugar returned to normal shortly after the initial determination. His sugar-tolerance test I inter-

pret as a normal curve. At the end of his first admission I feel that the diagnosis was cholecystitis, cholelithiasis and hemorrhagic pancreatitis.

He was treated conservatively on the first admission because we have found that patients with acute pancreatitis do much better if operation is postponed until localized signs of pancreatic abscesses are evident. The treatment in his case seems to have been very satisfactory as he was an extremely sick man on entry.

There are two points which I emphasize on his discharge following his first admission. One is that he had a mass in his epigastrium and the other that he had a van den Bergh of 3 mg. per cent. On his second admission, for some reason or other no mention is made of the mass. It probably had disappeared. X-ray at this time showed a high right diaphragm, and I should like to know if it moved for this would give a clue to subdiaphragmatic abscess. If so, it is not so stated in the x-ray report.

Dr. Tracy B. Mallory: There is no note about motion of the diaphragm.

Dr. Linton: At the end of the second admission I still think that the underlying disease is associated with his biliary tract. I think he undoubtedly had cholecystitis and cholelithiasis and developed a secondary pancreatitis which was treated by drainage.

I am rather surprised that no attempt was made to investigate his biliary tract on his first admission. That may have been because he was never in condition to warrant it. I think that a Graham test would have been positive if it had been done.

I am not quite certain of the cause of his death. I think that the episode involving both of his legs can be most likely accounted for by an acute arterial thrombosis. It certainly is not the picture of acute embolism. It is possible that it might be a dissecting aneurysm, but I doubt it as there is no sudden onset of pain that came before he noticed that his legs were cold and blanched. He certainly had arterial occlusion, which I think was an acute thrombosis at the bifurcation of the aorta, extending into the common iliac arteries. The fact that he did not get well makes me think there is a possibility of malignancy behind the whole story; that is, he might have malignancy involving the gall bladder and the gastrohepatic omentum. However, I favor a diagnosis of gall-bladder disease with gallstones and secondary pancreatitis with abscess formation. Secondary abscess formation that was not drained may have been the reason he came back the second time. In addition, I think he probably had an associated biliary cirrhosis.

Dr. Mallory: The question that struck us as particularly interesting and unusual in this case was that starting off with what was pretty obviously an acute hemorrhagic pancreatitis the patient winds up with ascites. Certainly that is an unusual complication of pancreatitis. I wonder if there are any suggestions.

Dr. Wyman Richardson: Portal vein thrombosis.

Dr. Mallory: That should be mentioned, certainly.

Dr. Linton: I do not believe that acute portal occlusion causes ascites.

Dr. Fuller Albright: He had no fever, which we thought was against portal thrombosis.

Dr. Mallory: Yes. What about the possibility of cirrhosis?

Dr. Albright: That was our diagnosis. We thought that he did have it, but why he had it we did not know. He looked like a person with Hanot's cirrhosis, but we could not see the connection. We considered portal thrombosis as a second choice.

Dr. Mallory: Chronic gall-bladder disease, which he had, would go with biliary cirrhosis, but that does not often cause ascites.

Clinical Diagnoses

Portal cirrhosis of liver.
Pancreatitis?
Portal thrombosis?
Thrombosis of both femoral arteries.

Dr. Linton's Diagnoses

Cholecystitis.
Cholelithiasis.
Hemorrhagic pancreatitis with secondary abscess formation.
Acute thrombosis at the bifurcation of the aorta extending into the iliac arteries.
Biliary cirrhosis.

Anatomic Diagnoses

Pancreatitis, acute, massive, gangrenous.
Peritonitis, acute, fibrinous, diffuse.
Compression of splenic, superior mesenteric and portal veins.
Ascites.
Fat necrosis, multiple, peritoneal and retroperitoneal.
Cholecystitis, chronic, with cholelithiasis.
Choledocholithiasis with dilatation of common duct.
Pulmonary atelectasis, focal, multiple.
Arteriosclerosis, moderate coronary; marked aortic, with ulceration.
Mural thrombus, abdominal aorta, with obstruction of common iliac arteries.
Necrosis of left adrenal.
Operative scars: incision and drainage of retroperitoneal abscess, and jejunostomy.

Pathological Discussion

Dr. Mallory: What we found at autopsy was exactly what Dr. Linton predicted, and it ade-

quately explained the ascites. The mass that was felt on the first examination and missed on the second, probably because of his ascites, was very large and consisted of remnants of pancreas, of the whole root of the mesentery and of the left adrenal, which had been completely destroyed. This mass completely surrounded the entire length of the splenic artery and vein, a portion nearly 3 cm. long of the superior mesenteric vein and a significant portion of the portal vein. The lumina of all these veins were clear so far as thrombosis was concerned, but they were very markedly narrowed by external pressure from the inflammatory mass. So I think that the ascites was primarily mechanical from portal obstruction, but without portal thrombosis. His relatively low serum protein level would, of course, have reinforced the mechanical element in its tendency to produce transudation. The cause of the arterial occlusion was, as Dr. Linton suggested, a thrombosis. There was a very large, deeply ulcerated, atheromatous plaque in the abdominal aorta just above the bifurcation and a large thrombus starting from it spread down into both iliac arteries. He had a distinctly thickened chronically inflamed gall bladder, which contained several stones, and three or four small stones were found in the common duct including one imbedded in the papilla. The liver itself was essentially negative.

CASE 23462

Presentation of Case

A thirty-eight-year-old, white, male factory worker entered the Emergency Ward with the complaint of abdominal pain and discomfort of four days' duration.

Four days before entry he began having sharp, cramplike, nonradiating pains in the midepigastrium. Within a few hours the pain had shifted to the right lower quadrant and had become steady and so severe that his physician gave him morphine for relief. When he attempted to move his bowels the pain radiated down into his rectum. The following day he was somewhat relieved but continued to have a sense of discomfort low in the middle of his abdomen. He did not vomit and continued to have a fair appetite. He was told by his physician that he had a temperature of 103°F., but he had no chills. The degree of pain remained relatively unchanged. He was constipated and had several enemas given to him. During the night before entry he had nocturia four times and some burning on urination. He had no other significant symptoms.

His past history and family history were essentially noncontributory. He had not had previous gastrointestinal symptoms.

Physical examination revealed an acutely ill, dehydrated man complaining of abdominal discomfort, centered in the lower part of the abdomen. The heart and lungs were negative. The blood pressure was 120 systolic, 80 diastolic. The abdomen showed spasm low in the midline and marked tenderness in the right lower quadrant, where a large mass was made out. Peristalsis appeared to be normal. Rectal examination revealed marked bulging of the anterior wall with exquisite tenderness and induration of the mucosa.

The temperature was 101.4°F., the pulse 80. The respirations were 20.

Urine examination showed a very slight trace of albumin. The blood showed a white cell count of 22,000. On the evening of the third day he had sudden severe sharp pain in both lower quadrants, more marked on the left. Shortly afterward an operation was performed. Through a low, muscle-splitting incision in the right side the peritoneal cavity was opened. The bowel and omentum were everywhere adherent, and no free fluid was visible. No exploration was done, but a large tube was sewed into the loop of bowel present in the right lower quadrant which appeared to be the terminal ileum. On the day of operation the blood showed a white cell count of 17,600, a nonprotein nitrogen of 32 mg. per cent and a serum protein of 4.5 gm. per cent. The chlorides were equivalent to 90 cc. of N/10 sodium chloride. He was Ochsnerized and given a transfusion, but his temperature and pulse remained high. A portable x-ray of his chest showed the diaphragm to be high in position, with poor aeration of the right lower lung field, diffuse haziness involving the lower two thirds of the left lung, but no displacement of the mediastinum. The ileostomy drained profusely, and peristalsis could be heard; however, his abdomen remained distended. On the sixth day the nonprotein nitrogen was 31 mg. and the protein 4.3 gm. per cent. The chlorides were equivalent to 86 cc. of N/10 sodium chloride; the CO_2 combining power was 56.5 vol. per cent. Another portable chest x-ray showed bilateral high diaphragms and some haziness in both lower lung fields, more marked on the left. On the following day his temperature rose to 103°F., his pulse to 130 and his respirations to 40. For the next week they remained at about these levels, fluctuating slightly. The white blood-cell count during this period varied between 12,000 and 23,000. On the seventh day he became somewhat irrational and was put into an oxygen tent. His abdomen became softer and peristalsis was easily heard. On the thirteenth day the van den Bergh was 3.67 mg. per cent, biphasic. A blood culture on the eleventh day was negative. A portable x-ray of the chest on the twelfth day showed that the diaphragm was lower in position. The right lung field was more radiant,

but there was still dulness in the left lung field. In spite of seven transfusions during his postoperative course, he died on the fourteenth hospital day.

Differential Diagnosis

Dr. Horatio Rogers: This case appears to be that of a man dying of bronchopneumonia, associated with sepsis originating in his abdomen. The onset is acute, without any previous gastrointestinal symptoms. As the onset is described it is more suggestive of acute appendicitis than anything else. It is entirely limited to the lower abdomen. The suggestion of urinary symptoms is not enough, I think, to make us consider the urinary tract as the original location of his trouble. It could conceivably be a bladder diverticulum which became infected and ruptured, causing an abscess low in the pelvis; but there is nothing on which to base any such suspicion except the presence of a pelvic abscess.

The record says that when he tried to move his bowels he had pain referred to the rectum. That does not make me think of the rectum as the primary focus of disease so much as it does of secondary involvement of the rectum by a pelvic abscess. Could it be diverticulitis — an inflammatory condition terminating fatally, causing, at one time at least, intestinal obstruction. It could be, except that there is nothing to lead up to it in the history. The onset is too acute, and comes out of a clear sky. Could it be regional ileitis? I cannot rule it out. The same process that is involving the appendix might involve the terminal ileum; but, again, there is nothing to back that up in the way of previous gastrointestinal disorders, which we should expect if this were a gradual process involving a large amount of intestine. Could it be any of the accidents, such as a volvulus or intussusception? For those, I should say that the onset was not sudden enough, and if they were untreated, we should expect them to go on to some degree of gangrene and make the patient sicker and die even quicker than he did.

As I reconstruct this picture it seems to me that he had acute appendicitis with a fairly typical onset. He received morphine for very acute pain, suggesting the type of acute appendicitis that is prone to rupture, possibly with a fecolith impacted in the appendix. The following day, after being relieved by morphine, the pain was less severe, suggesting that the appendix at that point ruptured, and the severe pain decreased. It was shortly thereafter that his temperature was said to be 103°F., and that straining at stool gave pain in the rectum, as it would have if by this time he had a beginning abscess in the pelvis.

On physical examination he obviously had an abscess low down in the pelvis with bulging of the anterior rectal wall, exquisite tenderness and high temperature and white count. Why he was not operated on at that point and an attempt made to drain the abscess through the rectum, does not appear. Later he was presumably operated on for intestinal obstruction, since his diaphragms were high and his abdomen distended, and the intestinal tract was decompressed by an ileostomy. It is interesting to speculate as to whether he then had a subdiaphragmatic abscess; this is suggested by the fact that the diaphragms did not go down to a normal level, particularly the left one. He continued to be very sick and died.

Should we consider cancer in this man? He is not too young, but I am assuming that his trouble was in the gastrointestinal tract, and it states clearly that there was no previous gastrointestinal history. I think that that rules out the possibility of this whole thing being a malignant process that perforated.

I shall have to say that this was acute appendicitis with rupture, localized peritonitis, later becoming a frank pelvic abscess, and death from bronchopneumonia and possibly a subdiaphragmatic abscess.

Dr. Aubrey O. Hampton: These films are postoperative. The first one was taken on the sixth day after operation, the second one day later, and the third six days from the first film. In the beginning his diaphragm was high on both sides with transverse lines across the base on the right and rather diffuse density in the region of the left lower lobe. His heart is not displaced appreciably; if anything it is toward the left. On the next day it seems as if there might be some improvement on the right and very little change on the left: and six days after the first examination the right lung is clear and the right side of the diaphragm has come down some, but the left side has gone up higher, and there are bands of density above it. It seems as though he must have had bilateral lower lobe collapse, either postoperative or due to the high diaphragm, which cleared on the right side and even improved considerably on the left; however, the diaphragm continued to go up on the left side in spite of the fact that the lungs cleared. So far as these portable films go they are quite consistent with left subphrenic abscess.

Clinical Diagnoses

Appendix abscess.
Generalized peritonitis.
Left subphrenic abscess?

Dr. Rogers's Diagnoses

Acute appendicitis with rupture.
Pelvic abscess.

Generalized peritonitis.
Bronchopneumonia.
Subdiaphragmatic abscess?

Anatomic Diagnoses

Perforated peptic ulcer (duodenal).
Peritonitis, generalized, acute purulent (alpha hemolytic streptococcus and *Bacillus coli*).
Peritoneal abscesses, multiple; left subphrenic and paracolic, pelvic, interintestinal, right paracolic and subphrenic.
Empyema, left.
Operative wound: terminal ileostomy.
Gastric erosion.
Pleuritis, chronic fibrous, bilateral.
Pulmonary congestion and atelectasis.
Arteriosclerosis, minimal, aortic and coronary.

Pathological Discussion

Dr. Tracy B. Mallory: Dr. Rogers has made what seems to be the obvious and rational diagnosis. It was the diagnosis made in the house. They thought he had an appendix abscess. They felt at the time they operated, however, that obstruction was the immediate cause of most of his symptoms. They expected the abscess to point eventually in the rectum but preferred to give it a little more time to wall off before attempting to drain it. The autopsy, however, showed that there was no appendicitis. He had a perfectly normal appendix, but there was a perforated duodenal ulcer which was undoubtedly the cause of the peritonitis. The suddenness with which the symptoms localized in the right lower quadrant and the rectum makes it an exceptional case and worth bringing up, even if it is a little hard on Dr. Rogers. Furthermore, I do not think I should let the x-ray department off scot-free, as there was 1000 cc. of pus in the left pleural cavity.

Dr. Hampton: How long after that last film did he die?

Dr. Mallory: Not very long, three days.

Dr. Grantley W. Taylor: Was there a localized collection of pus under the left diaphragm?

Dr. Mallory: Yes. There were pockets of pus throughout the peritoneal cavity. About four large separate abscesses were described in the protocol, but there were such numerous small ones that one could practically call it a diffuse peritonitis. The lungs showed extensive collapse at the bases, particularly on the left where the empyema was found.

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MORE ON "PRINCIPLES AND PROPOSALS"

The furor created by the recently released "Principles and Proposals" regarding medical care seems extremely unfortunate, but nevertheless justified. As originally published in the *Journal of the American Medical Association* without the committee's explanation of their origin and purpose, these resolutions to govern future medical policies fail to include direct mention of the medical profession or the individual physician. Hence, one can hardly blame the practitioner for becoming upset. On the other hand, the proponents of these principles and proposals have a right to be annoyed when they are accused of promoting the very thing — state medicine — that they are trying to avoid. Although both groups have cause for their mental reactions, the true state of affairs seems to be one of misunderstanding rather than one based on radically opposed points of view.

Several matters enter into consideration. In the first place, it must be acknowledged that many of the indigent do not receive proper medical care. This does not apply particularly to Massachusetts, but it is certainly true in many sections of the country. To provide such care is the concern of government — local, state or federal, preferably in the order listed; this does not mean "state medicine" but merely that physicians and hospitals that actually furnish the treatment are paid for their services through funds collected from the taxpayers. Furthermore, good as medical care is in this country, there is room for improvement.

To a social-security-minded administration such a condition should be corrected, and admittedly, the need seems to be greater than that of many of the "reforms" fostered by said administration. It is understood that a bill to "correct" the situation has been written and that the individuals rightly qualified to give advice were not consulted. Possibly the bill embraces health insurance as provided by the recently inaugurated Group Health Association in Washington or it may even be as radical as the proposals which Senator Lewis expounded at the Atlantic City meeting of the American Medical Association. Whatever it was — or is — it assuredly did — or does — not coincide with the views held by the majority of the medical profession, and it was to prevent any such precipitous and unwise legislation, tending to disrupt the present organization of medical care, that a group of physicians was organized. They apparently felt that it was better to formulate a definite policy rather than to adopt a laissez faire attitude, such as that of the American Medical Association.

For this purpose the "Principles and Proposals" came into existence. If one carefully considers the names included in the committee that was responsible for the plan and among those four hundred physicians who signed it, it is difficult to believe that men of this caliber would be willing

to sponsor any plan which they did not honestly believe would be advantageous to the medical profession. If this is the case, why is there such marked disagreement among the members of the profession in regard to the plan?

The chief trouble seems to arise from the wording of the "Principles and Proposals." By themselves they certainly connote "government medicine." It is difficult to believe that this is the meaning really implied, and it is unfortunate that they were presented in this form in the *Journal of the American Medical Association*. The statement by the committee which precedes the "Principles and Proposals" eliminates some of the objections, but even a more detailed explanation or a rewording seems desirable if the practitioner is to appreciate what the "Principles and Proposals" represent. Let us try to restate and add to them so that they appear less objectionable.

PRINCIPLES

1. That the health of the people is a direct concern of the country.
2. That a national public health policy, including preventive medicine, care of the indigent, medical education, food and drug control, and so forth, should be formulated.
3. That the problems of economic need and of providing medical care are not identical and require different approaches for their solution.
4. That in the provision of adequate medical care for the population five agencies are essential and their importance lies in the order named: the medical profession, voluntary agencies, and local, state and federal governments.
5. That neither compulsory health insurance nor the regimentation of physicians offers a satisfactory solution to the problem.

PROPOSALS

1. That the first necessary step toward the realization of the above principles is to minimize the risk of illness by prevention.
2. That an immediate problem is provision of adequate medical care for the indigent, the cost to be met from public funds (local and/or state and/or federal).
3. That public funds should be made available for the support, with the view to improvement, of medical education and for studies, investigations and procedures for raising the standards of medical practice. If this is not provided for, the provision of adequate medical care may prove impossible.
4. That public funds should be available for medical research as essential for high standards of practice in both preventive and curative medicine.
5. That public funds should be made available to hospitals that render service to the indigent and for laboratory and diagnostic and consultative services.
6. That in allocation of public funds existing private institutions should be utilized to the largest possible extent and that they may receive support so long as their service is in consonance with the above principles.
7. That public health services, local, state and federal, should be extended by evolutionary process.
8. That the investigation and planning of the measures proposed and their ultimate direction should be assigned the medical profession with the co-operation, when necessary, of economists and sociologists.
9. That the adequate administration and supervision of the health functions of the government, as implied in the above proposals, necessitates in our opinion a functional consolidation of all federal health and medical activities, proferably under a separate department.

This redraft may not truly represent the ideas promulgated by the committee, but it seems to cover all the points contained in the original "Principles and Proposals" and at the same time eliminates some of the objections.

NATIONAL MILK WEEK

THE production of quality milk has come a long way forward since the day when the most important individual member of any herd was "the cow with the iron tail"—the barnyard pump. Esthetic sensibilities also, particularly in urban areas, have developed tastes in milk that do not require that tang which an early producer of clean milk offered to supply by dispensing with his product tea bags of dried manure that customers could use according to individual preference.

Early legal standards set requirements only for the nutritive value of milk, which banished from the herd the cow with the iron tail, established minimum percentages of butter fat and attempted to prevent adulteration. It was not until the role of bacteria in disease became well established as a fact, and particularly the part that the tubercle bacillus plays in jeopardizing the health of both cow and man, that the importance of milk as a culture medium for divers organisms and as a

transmitting agent for tubercle bacilli began to be seriously considered.

In view of certain startling discoveries by Robert Koch in 1882, the General Court of Massachusetts, perhaps somewhat tardily, in 1895 passed an act requiring the compulsory tuberculin testing of cattle in the State. When it became apparent that from 30 to 50 per cent of our cows were being destroyed as tuberculous, economic factors came into play, and the act was naturally and in short order repealed. In 1906 the first dairy inspection by the State Board of Health was established, but not without long-continued and irate protest from the embattled farmers.

In 1910 the Federal Bureau of Animal Industry took up this eradication of bovine tuberculosis in the District of Columbia, and legislation in 1917 put the *accreditation* of herds and areas on a nation-wide footing. This noteworthy work has continued to the present time, although lately the retesting of herds has lagged, possibly because this method of livestock destruction has not kept pace with the demands of a modern era.

The certified milk plan, however, antedates all these efforts in the direction of an improved milk supply, having been introduced in 1892, and the National Association of Medical Milk Commissions was formed in 1906. The quantity of certified milk produced has always been but a small percentage of the total supply, but aside from its value as an infant food, it has furnished an unalterably steadfast object lesson of proper methods of production. When, in recent years, Boston led the way in the pasteurization of certified milk, the final seal of honest approval was put upon it.

National Milk Week must undoubtedly have its value in promoting the honest sale, for honest purposes, of honestly produced milk, and the *Journal* is pleased to back it to that extent. We must confess, however, to being a little tired of slogans; a little wearied by claptrap. Clean milk is a valuable food at any age and almost indispensable in infancy. It is not, however, a complete food, beyond the early months of infancy, and to compare its value with that of a pound of lean beef or with three and one-third pounds of oysters has no particular meaning unless we know just what qualities we are trying to compare. Milk is undoubtedly a most useful food, and more of it should be consumed, but not by way of a debauch.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY

M. Fletcher Eades, M.D., *Secretary*
19 Bay State Road
Boston

Case History No. 46. Complete Placenta Previa; With Cesarian Section, at Seven and a Half Months

Mrs. F. B., an American housewife, aged thirty, a primipara, was seen in the hospital on June 30, 1929, in consultation. She had flowed three or four days previously when she was almost six months pregnant.

Her father was an invalid; her mother, one brother and a sister were alive and well. There was no history of tuberculosis, hemorrhagic disease or malignancy.

The patient's past history was negative. She had had no children's diseases or operations. Catamenia began at twelve, were of the twenty-eight-day variety, and lasted from two to five days with no real pain. Her last period was December 25, which would make the baby due the very end of September.

She was a well-developed and nourished woman. Her heart showed no enlargement and no murmurs. The lungs were resonant throughout, and there were no rales. The extremities were negative. Her breasts were enlarged, showing changes compatible with pregnancy. Her blood pressure was 110 systolic, 60 diastolic. The uterus was the size of a six months' pregnancy. The fetal heart was distinctly heard, and the breech presented. There was no flowing at the time she was seen, and no vaginal examination was made. It was advised that she stay in the hospital and be examined subsequently.

Vaginal examination was made four days later. The cervix was not obliterated but it was soft. No attempt was made to invade the cervical canal. No definite diagnosis of placenta previa was made.

The patient left the hospital two days after the vaginal examination; she led a quiet life and did not flow again until August 14. At this time she flowed a great deal, enough to saturate her clothing; there was no pain. She was advised to go into the hospital immediately.

A series of selected case histories by members of the section will be published weekly.

Comments and questions by subscribers are solicited and will be discussed by members of the section.

On physical examination her pulse was found to be 90. The fetal heart was distinctly heard. Her blood pressure was 112 systolic, 60 diastolic. On palpation the uterus was perfectly soft, and there was no tenderness. The breech was presenting, and a presumptive diagnosis of partial separation of the placenta was made, possibly some type of placenta previa. The softness of the uterus plus the perfectly definite fetal heart ruled out an entirely separated placenta. There was no attempt to make an exact diagnosis as the bleeding had ceased. A blood test proved the patient's blood to be compatible with that of her husband.

Two days later, however, the patient started to bleed very freely; since she was not in labor, it was felt that cesarian section was the operation of choice. A classical cesarian was done, and no difficulties were encountered. The baby weighed 4 lb., 9 oz. The placenta was found to be lying entirely over the cervix — a complete placenta previa. The placenta after its delivery showed an area of old adherent blood clot, evidence of the site of previous separation. Convalescence was complicated by a stitch abscess. The patient was discharged from the hospital at the end of three weeks; the baby was nursing.

Comment. The treatment of patients who bleed during pregnancy primarily means hospitalization. If, as in this case, the pregnancy when bleeding occurs is only in the seventh month, it is wise to defer examination unless the bleeding persists. If the bleeding persists, a definite diagnosis must be made, and proper treatment instituted.

This patient was allowed to go home and be up and about. It would probably have been better obstetrics if, after the bleeding had ceased and the examination had revealed nothing, she had been kept in bed.

It is not easy to make a diagnosis of complete placenta previa unless the patient is in labor, and it is unwise before viability to attempt to invade the cervix to establish a diagnosis because of the possibility of starting hemorrhage prematurely and losing the baby.

Active bleeding, irrespective of whether the fetus is viable or not viable, demands immediate treatment. Intelligent procrastination, when bleeding has ceased, for the purpose of obtaining a viable child, so long as the patient is in the hospital where delivery can be accomplished at any time, is warranted.

Cesarian section was done on this case for the following reasons: breech presentation, active bleeding, no labor. The position of the placenta — complete previa — proved the wisdom of this course.

POSTGRADUATE EXTENSION COURSES

The postgraduate extension courses for all registered physicians of the Commonwealth of Massachusetts will be given under the auspices of the Massachusetts Medical Society. The courses will be sponsored jointly by the Society, the State Department of Public Health, the United States Public Health Service and the Federal Children's Bureau.

The courses will begin in some districts early in January; while other districts will have the courses in the spring. This plan has been made because of the arrangements necessary to organize material for courses and other details.

The extension courses will begin in January, 1938, in the following places:

District	*Place*
Bristol North	Taunton
Bristol South	New Bedford
Essex South	Salem
Middlesex East	Melrose
Middlesex North	Lowell
Middlesex South	Cambridge
Norfolk	Norwood
Norfolk South	Quincy
Plymouth	Brockton
Worcester	Milford
Worcester North	Fitchburg

The extension courses will begin in the early spring of 1938 in the following places:

District	*Place*
Barnstable	Hyannis
Berkshire	Pittsfield
Bristol South	Fall River
Essex North	Haverhill
Franklin	Greenfield
Hampden	Springfield
	Holyoke
Hampshire	Northampton

The courses and chairmen in charge are as follows:

Course	*Chairman in Charge*
Gonorrhea	Dr. E. Granville Crabtree
Syphilis	Dr. E. Granville Crabtree
Heart Disease	Dr. Paul D. White
Rheumatic Fever	Dr. Paul D. White
Obstetrics	Dr. Robert L. DeNormandie
Pediatrics	Dr. Warren R. Sisson
Pneumonia	Dr. Frederick T. Lord

For further information see your district chairmen whose names are as follows:

District	*Chairman*
Barnstable	Dr. John I. B. Vail
Berkshire	Dr. Melvin H. Walker, Jr.
Bristol North	Dr. Arthur R. Crandell

Bristol South	
Fall River	Dr. Howard P. Sawyer
New Bedford	Dr. Robert H. Goodwin
Essex North	(To be announced later)
Essex South	Dr. Walter G. Phippen
Franklin	Dr. Halbert G. Stetson
Hampden	
Holyoke	Dr. George D. Henderson
Springfield	Dr. George L. Schadt
Hampshire	Dr. Robert B. Brigham
Middlesex East	Dr. Joseph H. Fay
Middlesex North	Dr. William S. Lawler
Middlesex South	Dr. Edmund H. Robbins
Norfolk	Dr. Hugo B. C. Riemer
Norfolk South	Dr. David L. Belding
Plymouth	Dr. Walter H. Pulsifer
Worcester	
Milford	Dr. Joseph Ashkins
Worcester North	Dr. Edward A. Adams

Full details about the course and programs will be mailed to each doctor in the State early in December.

Dr. Reginald Fitz, *Chairman,*
Dr. Frank R. Ober,
Dr. Joseph W. O'Connor,
Dr. Robert N. Nye,
Dr. Leroy E. Parkins, *Secretary,*
Executive Committee on
Postgraduate Instruction.

"GREEN LIGHTS TO HEALTH"

The balance of the 1937 program of the broadcasts "Green Lights to Health," sponsored by the Massachusetts Medical Society and the Massachusetts Department of Public Health and given through the courtesy of Station WAAB at 7:30 p. m. on the dates mentioned, is as follows:

November 17 — What Strong Emotions Do to Us. Dr. Walter B. Cannon.
24 — Nature's Barometer of Health — the Mouth. Dr. Leroy M. S. Miner.

December 1 — Shoes and Feet. Dr. Lloyd T. Brown.
8 — Group Hospitalization in Massachusetts. Dr. Joseph B. Howland.
15 — Asthma. Dr. Francis M. Rackemann.
22 — How to Keep Your Eyesight in Trim. Dr. Hugo B. C. Riemer.
29 — Colds and What To Do About Them. Dr. George P. Reynolds.

MISCELLANY

APPOINTMENT OF DR. JOSEPH E. BARRETT

Dr. Joseph E. Barrett, of Taunton, has been appointed director of the State Hospital Commission of Michigan by Governor Frank Murphy and the newly created commission. The State of Michigan has recently adopted important and progressive legislation dealing with the care of the insane, embodying a broad mental hygiene program and creating a central State Hospital Commission with a director as chairman.

Dr. Barrett was born in Jonesboro, Arkansas, April 24, 1891, and was educated in the public schools of that city and in the State University. He graduated from the University of Tennessee College of Medicine in 1922 and served a rotating internship at the St. Louis General Hospital. He was assistant physician at the State Hospital for nervous diseases, Little Rock, Arkansas, from 1923 to 1928. He was appointed assistant superintendent of the Taunton State Hospital, Taunton, in 1928, promoted to assistant to the commissioner in the Massachusetts Department of Mental Diseases in 1931 and to assistant commissioner in 1934. He resigned June 1, 1937, since which time he has been engaged by the National Committee for Mental Hygiene in making surveys of state hospitals in Iowa and Virginia. He is a member of the Massachusetts Medical Society, a fellow of the American Medical Association and American Psychiatric Association, a member of the New England Society of Psychiatry, the Massachusetts Psychiatric Society and the National Committee for Mental Hygiene, and a diplomate of the American Board of Psychiatry and Neurology.

Dr. Barrett's resignation as assistant commissioner in the Massachusetts Department of Mental Diseases last June was subsequent to replacement of Dr. Winfred Overholser, of Wellesley, as commissioner of the department. Massachusetts can ill afford such an exodus of psychiatric talent, which recently included the appointment of Dr. Overholser as superintendent of St. Elizabeths Hospital, Washington, D. C.

DR. CURTIS APPOINTED GRENFELL HEAD

Dr. Charles S. Curtis, a native of Shrewsbury, a graduate of Harvard Medical School and a former intern at the Boston City Hospital, has been recently appointed medical superintendent and executive officer of hospitals and schools conducted on the coasts of Labrador and northern Newfoundland by the International Grenfell Association. These institutions include five hospitals, six nursing stations, three hospital ships and several schools.

CONNECTICUT NEWS

State Aid for Crippled Children

Under the Social Security Act, Connecticut will receive $60,000 from the federal government to be added to another $60,000 appropriated by the last session of the General Assembly for the Crippled Children's Aid program. The State Department of Health has worked out an integrated and far-reaching plan for providing health services to crippled children in areas predominantly rural or suffering from economic distress. Five permanent diagnostic clinics will be strategically located throughout the State so that they may be accessible to districts where their services are most needed. Aftercare treatment at home will be carried out by arousing the interest of agencies other than the State Department of Health and by giving the parents adequate knowledge of what is required.

The Medical Information Bureau

The joint Medical Information Bureau of the Hartford County Medical Association and the Hartford (City) Medical Society is now prepared to furnish the public the names of physicians who will provide professional services upon request. It is believed that this will be a great con-

venience to new residents, temporary residents, visitors, persons en route through Hartford, and others who in the past have had difficulty in locating a physician. The names are selected on a geographical basis, the patient being furnished with the names and telephone numbers of the three listed member physicians whose home addresses are nearest the patient. The actual contacting of the physician selected by the patient must be done by the latter.

Semiannual County Meetings

The New London County Association met on October 7 at Uncas-on-Thames, Norwich, to listen to a paper on "The Treatment of Neurosyphilis" by Dr. Samuel Epstein, of Harvard Medical School. This was preceded by dinner and a business session.

Middlesex County Association held its meeting on the Wesleyan University campus on October 12. A business session preceded the dinner. Dr. Richard H. Overholt, of Boston, was the guest speaker, his subject being "Surgical Diseases of the Chest."

The one hundred and forty-fifth semiannual meeting of the Tolland County Association was held in Somers on October 19. The usual business session followed the dinner. Dr. C. C. Burlingame, of Hartford, presented a paper on "Psychiatry in Medicine."

The Windham County Association met in Willimantic on October 21. Following the dinner and business session Dr. Frank S. Jones, of Hartford, presented the subject of "Compression Fractures of the Spine." There was considerable discussion of this interesting paper.

The Hartford County Association meeting in Manchester on October 26 afforded its members an afternoon of golf, a delightful dinner, and two papers. The first was a short one on the "Presentation of a Splint" by Dr. Le Verne Holmes. The other was a presentation of the interesting problem of the training of surgeons to meet the requirements of the newly formed American Board of Surgery by Dr. Arthur W. Elting, professor of surgery, Albany Medical College. Dr. Elting styled his address "Keeping Up with Medical Practice."

The final county meeting was that of the New Haven Association on October 28 at Waterbury. Many enjoyed golf in spite of the weather. The afternoon program consisted of a business session followed by a paper on "Discussion of *American Medicine: Expert Testimony Out of Court*" by Dr. Robert B. Osgood, emeritus professor of orthopedic surgery, Harvard Medical School. "The Doctor and Health Insurance" was then presented by Dwight Anderson, director, Public Relations Bureau of the New York State Medical Society. Both papers were discussed together. Following a dinner the members listened to Dr. Robert H. Lowie, exchange professor of anthropology, Leland Stanford University.

PUBLIC HEALTH FELLOWSHIPS

Fellowships for graduate work at the Harvard School of Public Health, as provided by a program of study financed by the U. S. Public Health Service, have been recently granted to seven members of the Boston Health Department. The holders are as follows: Dr. Frederick J. Bailey, of Dorchester, deputy commissioner in charge of communicable diseases; Dr. Karl Bailey, of Brookline, deputy commissioner in charge of the laboratory division; Drs. John H. Cauley, of Dorchester, and Harry Goldman and George Kahn, of Boston, medical inspectors in charge of the city health units; Dr. George O'Donnell, of Newton, deputy commissioner in charge of the division of tuberculosis; and Miss Hazel Wedgwood, of Boston, director of the nursing service.

MAINE NEWS

During the annual clinical session of the Maine Medical Association held this year October 21 and 22 in Portland, a meeting of the State Cancer Committee was held, at which Drs. William Holt, of Portland, Magnus Ridlon and Forrest Ames, of Bangor, Ernest Call of Lewiston, and Edward Risley, of Waterville, were present. It was voted:

1. To approve the Tumor Clinic at the Sisters' Hospital in Waterville.
2. To approve the dates, April 2 to 9, 1938, for the next educational campaign of the Women's Field Army.
3. That the Cancer Committee recommend to each county society that at least one meeting a year be devoted to the subject of cancer. The programs are to be arranged by the Cancer Committee if requested.

At a meeting of the Advisory Committee of the Women's Field Army, Maine State Division of the American Society for the Control of Cancer, Dr. Edward Risley, of Waterville, was elected chairman.

CORRESPONDENCE

AN APPEAL FOR FITZIANA

November 10, 1937.

To the Editor: I am engaged in the gathering of material for a biography of Reginald Heber Fitz (1843-1913). The *Journal* may be of assistance in reaching readers who had the privilege of knowing Dr. Fitz personally or who may have some of his correspondence. I shall be grateful for any help, and will be responsible for the safe return of any letters sent to me.

Hyman Morrison, M.D.

483 Beacon Street,
Boston.

RECENT DEATHS

GODDU — Louis A. O. Goddu, M.D., died November 11 at his home, 40 Abbottsford Road, Brookline, after a brief illness. He was in his fifty-ninth year.

A graduate of the Massachusetts College of Pharmacy and Tufts College Medical School, he served internships at the Carney and Massachusetts General hospitals. Dr. Goddu was formerly chief orthopedic surgeon at the state hospital in Woonsocket, Rhode Island, and served in an advisory capacity at the Lakeville and Pondville hospitals. At the time of his death he was assistant professor of orthopedic surgery at Tufts College Medical School, orthopedic surgeon-in-chief at the Boston Floating Hospital and Roxbury Hospital, and was for many years on the orthopedic staff of the Massachusetts General Hospital.

Among his affiliations were memberships in the American College of Surgeons, the Boston Orthopedic Club and the University Club of Boston. He held fellowships in the Massachusetts Medical Society and the American Medical Association.

His widow, the former Jessie Abercrombie, and a daughter, Margaret, survive him.

MAHONEY — GEORGE C. MAHONEY, M.D., of 97 College Avenue, West Somerville, died November 9 at his home. He was in his seventy-third year.

Dr. Mahoney graduated in 1894 from Bowdoin Medical School. He was a practicing physician in Somerville for more than forty years.

Among his affiliations were memberships in the Masonic Order, the Bowdoin Club of Boston, and the Sons of Maine. He was a fellow of the Massachusetts Medical Society and of the American Medical Association, and a member of the Somerville Medical Society.

ANDREWS — EDWARD AUSTIN ANDREWS, M.D., of Newton, died November 8, at the Newton Hospital. He was in his sixty-seventh year.

A native of Whetmore, Kansas, he was graduated from Harvard Medical School in 1896. He was a former staff member of the Boston Children's Hospital and for twenty-five years was on the staff of the Newton Hospital.

Dr. Andrews was the chairman of the Newton Library Committee, a member of the Mayor's Relief Committee and for sixteen years president of the Newton Center Improvement Association. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow and a son survive him.

BLAIR — GEORGE K. BLAIR, M.D., of 311 Essex Street, Salem, died November 3 at the Salem Hospital. He was in his sixty-third year.

A native of Boothbay, Maine, he was graduated from Bowdoin College and received his degree from Bowdoin Medical School in 1900.

Dr. Blair held fellowships in the Massachusetts Medical Society and the American Medical Association, and was a member of the Masonic Order. From 1903 to 1908 he was a member of the Salem school committee.

His widow survives him.

REPORTS OF MEETINGS

WACHUSETT MEDICAL IMPROVEMENT SOCIETY

A meeting of the Wachusett Medical Improvement Society was held on November 3 at the Holden District Hospital. Dinner was served at 6:30 p. m., followed by a scientific program at 7:30 p. m.

Dr. Joseph Muller, of Worcester, spoke on "Who Shall Treat Syphilis and How" and Dr. William A. Hinton, chief of the Wassermann Laboratory, Boston, spoke on "Laboratory Blood Serum and Its Interpretation."

MASSACHUSETTS PSYCHIATRIC SOCIETY

The Massachusetts Psychiatric Society held its annual dinner meeting at the Parker House on Friday evening, October 8. Dr. John C. Whitehorn, of McLean Hospital, gave the address of the evening.

The following officers were elected for the coming year: Dr. Clarence A. Bonner, president; Dr. Harry C. Solomon, vice-president; Dr. W. Franklin Wood, secretary-treasurer; Dr. Oscar J. Raeder and Dr. William A. Bryan, councilors.

NOTICES

LAWRENCE CANCER CLINIC

The regular Lawrence Cancer Clinic, to be held at the Lawrence General Hospital, 1 Garden Street, Lawrence, on Tuesday, December 7, at 10:00 a. m., will be a demonstration and teaching clinic for physicians, with Dr. Channing C. Simmons, of Boston, associate in surgery in the graduate courses in medicine at Harvard Medical School, surgeon-in-chief to the Collis P. Huntington Memorial Hospital, member of the Cancer Commission of Harvard University, and visiting surgeon to the Massachusetts General Hospital, present as consultant. Physicians of the north half of Essex County are invited to accompany any of their patients whom they desire to have this service or to send them with a note. A report will be returned to every physician who sends a patient. The service is gratis. Any physician is welcome to attend the clinic.

This clinic is endorsed by the Committee on Postgraduate Instruction of the Massachusetts Medical Society.

ROY V. BAKETEL, M.D.,
CHARLES J. BURGESS, M.D.,
JOHN J. MCARDLE, M.D.,
HARRY H. NEVERS, M.D.,
THOMAS V. UNIAC, M.D.,
J. FORREST BURNHAM, M.D., *Chairman.*

MOTION PICTURE: THE DIAGNOSIS AND TREATMENT OF SYPHILIS

On Tuesday, November 23, at 4:45 p. m., in Amphitheater E, Harvard Medical School, there will be a showing of the motion picture entitled "Diagnosis and Treatment of Syphilis" under the auspices of the Department of Dermatology and Syphilology of the Harvard Medical School.

This film was produced under the joint auspices of the American Medical Association and the United States Public Health Service, and shows national authorities on the subject.

The lecturers in the film are Dr. John H. Stokes on the diagnosis of early syphilis; Dr. Harold N. Cole on the treatment of syphilis; Dr. Paul A. O'Leary on latent syphilis; Dr. Philip C. Jeans on congenital syphilis; and Dr. Joseph E. Moore on neurosyphilis.

SCIENTIFIC EXHIBIT: AMERICAN MEDICAL ASSOCIATION

Application blanks are now available for space in the Scientific Exhibit at the San Francisco session of the American Medical Association, June 13 to 17, 1938. The Committee on Scientific Exhibit requires that all applicants fill out the regular forms.

Application blanks may be obtained from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago, Illinois.

THE BOSTON DISPENSARY

There will be a luncheon meeting of the clinical staff of the Boston Dispensary on Tuesday, November 23, in the auditorium on the second floor of the Dispensary building, at 12:00 noon.

At 12:30 p. m., Dr. George R. Minot will talk on the subject: "Anemia: Etiology, Diagnosis and Treatment."

An invitation is extended to any who are interested in the subject. Luncheon to non-members is 35 cents.

ALLEN R. BARROW, M.D., *Secretary.*

BERKSHIRE DISTRICT MEDICAL SOCIETY

The next meeting of the Berkshire District Medical Society will be held at the Wendell Hotel on November 22 at 6:30 p. m.

The speaker will be Dr. Walter Dandy, associate professor of surgery, Johns Hopkins Hospital. His subject will

be "Care of Injuries to the Head." Dr. Eldridge Campbell, neurosurgeon of the Albany Hospital, will discuss the paper.

HUGH DOWNEY, M.D., *Secretary.*

THE BOSTON SOCIETY OF ANESTHETISTS

The next meeting of the Boston Society of Anesthetists will be held at the Hotel Kenmore, on Tuesday, November 23. (Note change of date.)

Dinner at 6:30 p. m.

Business meeting at 7:40 p. m.

Scientific program at 8:00 p. m.

Report of Meeting of Anesthetists' Travel Club.
Report of Interesting Cases. Dr. Ralph Tovell.

ELEANOR B. FERGUSON, M.D., *Secretary.*

NEW ENGLAND HEART ASSOCIATION

The next meeting of the New England Heart Association will be held at the Massachusetts General Hospital, Monday, November 22, at 8:15 p. m.

PROGRAM

Further Observations on the Healing of Myocardial Infarction. Dr. G. Kenneth Mallory and Dr. Paul D. White.

The Clinical Value of the Estimation of the Volume of the Heart as Determined by Orthodiography. Dr. Wilfrid J. Comeau and Dr. Paul D. White.

Electrocardiograms on Identical Twins. Dr. M. Bowman Wise and Dr. Wilfrid J. Comeau.

A Series of Cases in Which the Electrocardiographic Lead from the Cardiac Apex Was the Chief Diagnostic Aid in Coronary Thrombosis. Dr. Howard B. Sprague.

The Effect of Early Treatment of Lues on the Later Appearance of Aortic Lues. Dr. Wilfrid J. Comeau, Dr. William P. Thompson, and Dr. Paul D. White.

Long Survival of Patients with Aneurysms of the Aorta. Dr. Edward F. Bland.

All members of the New England Heart Association and interested physicians are invited to attend.

JAMES M. FAULKNER, M.D., *Secretary.*

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held in the Peter Bent Brigham Hospital Amphitheater (Shattuck Street Entrance), Tuesday, November 23, at 8:15 p. m.

PROGRAM

Presentation of Cases.

Pyelonephritis: Its relation to arterial hypertension and to Bright's disease. Dr. Soma Weiss.

Medical students and physicians are cordially invited to attend.

MARSHALL N. FULTON, M.D., *Secretary.*

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, NOVEMBER 22

MONDAY, NOVEMBER 22

*8:15 p. m. New England Heart Association. Massachusetts General Hospital.

TUESDAY, NOVEMBER 23

*9 a. m. - 10 a. m. Boston Dispensary. X-ray demonstration. Boston Floating Hospital cases. Dr. Alice Ettinger.

*12 m. Boston Dispensary. Clinical staff meeting. Second floor.

*4:45 p. m. Harvard Medical School; Amphitheater E. Motion picture "The Diagnosis and Treatment of Syphilis."

8 p. m. Boston Society of Anesthetists. Hotel Kenmore, Boston.

*8:15 p. m. Harvard Medical Society. Peter Bent Brigham Hospital Amphitheater (Shattuck Street Entrance).

WEDNESDAY, NOVEMBER 24

*9 a. m. - 10 a. m. Boston Dispensary. Hospital case presentation. Dr. S. J. Thannhauser.

*12 m. Clinicopathological conference. Children's Hospital Amphitheater.

*12 m. Boston Society for the Advancement of Gastroenterology. Amphitheater of the Peter Bent Brigham Hospital.

FRIDAY, NOVEMBER 26

*9 a. m. - 10 a. m. Boston Dispensary. Angina Pectoris and Coronary Sclerosis. Dr. Samuel A. Levine.

SATURDAY, NOVEMBER 27

*9 a. m. - 10 a. m. Boston Dispensary. Hospital case presentation. Dr. S. J. Thannhauser.

*10 a. m. - 12 m. Staff rounds at the Peter Bent Brigham Hospital. Conducted by Dr. Henry A. Christian.

*Open to the medical profession.

NOVEMBER 18 — Pentucket Association of Physicians. Hotel Bartlett, 95 Main Street, Haverhill, 8:30 p. m.

NOVEMBER 18 — New England Pathological Society. Page 802, issue of November 11.

NOVEMBER 18 — Boston Society of Psychiatry and Neurology. Page 802, issue of November 11.

NOVEMBER 18 — Robert Breck Brigham Hospital meeting. Page 801, issue of November 11.

NOVEMBER 22 — New England Heart Association. Notice above.

NOVEMBER 23 — Harvard Medical Society. Notice above.

NOVEMBER 23 — The Boston Society of Anesthetists. Notice above.

NOVEMBER 23 — Motion Picture "The Diagnosis and Treatment of Syphilis," Harvard Medical School. Page 849.

NOVEMBER 23 — Boston Dispensary. Clinical staff meeting. Page 849.

NOVEMBER 24 — The Boston Society for the Advancement of Gastroenterology. Page 801, issue of November 11.

DECEMBER 7 — Lawrence Cancer Clinic. Page 849.

DECEMBER 7 - MAY 3 — Greater Boston Medical Society. Page 762, issue of November 4.

DECEMBER 20 — Boston Medical History Club. 8:15 p. m. Boston Medical Library.

APRIL 4-8, 1938 — The American College of Physicians. Page 41, issue of July 1.

DISTRICT MEDICAL SOCIETIES

BERKSHIRE

NOVEMBER 22 — Page 849.

BRISTOL SOUTH

MAY 5, 1938 — 5 p. m., New Bedford.

ESSEX SOUTH

DECEMBER 1 — Salem Hospital. Clinic at 5 p. m. Dinner at 7 p. m. Speaker: Dr. Leland S. McKittrick. Subject: Carcinoma of Colon. Discussion of Diagnosis.

JANUARY 5 — Danvers State Hospital. Clinic at 5 p. m. Dinner at 7 p. m. Speaker and subject to be announced.

FEBRUARY 2 — Council Meeting, Boston.

FEBRUARY 9 — Essex Sanatorium, Middleton. Clinic at 5 p. m. Dinner at 7 p. m. Speaker: Dr. John B. Hawes, 2nd. Subject: Dust and Disease.

MARCH 2 — Lynn Hospital. Clinic at 5 p. m. Dinner at 7 p. m. Speaker and subject to be announced.

APRIL 6 — Gloucester Hospital, Gloucester. Clinic at 5 p. m. Dinner at 7 p. m. Speaker and subject to be announced.

MAY 5 — Censors meet at Salem Hospital, 3:30 p. m.

MAY 11 — Annual meeting, Salem Country Club, Peabody. Dinner at 7 p. m. Speaker and subject to be announced.

FRANKLIN

Meetings will be held at the Franklin County Hospital, Greenfield, at 11 a. m. the second Tuesdays of January, March and May.

HAMPDEN

Meetings will be held on the fourth Tuesday in January, April and July.

MIDDLESEX EAST

Meetings will be held at the Bear Hill Golf Club, Stoneham, at 12:15 p. m. on January 12, March 16, and May 11.

MIDDLESEX NORTH

Meetings will be held at the Vesper Country Club, Lowell, on January 26, and April 27.

NORFOLK DISTRICT

November 30 — Hotel Kenmore. 8:15 p. m. Diagnosis of Lesions of the Hand with Demonstration of Patients. Dr. William E. Browne.

January 25 — Hotel Kenmore. 8:15 p. m. The Management of Uterine Prolapse. Dr. Louis E. Phaneuf.

February 23 — Hotel Kenmore. 8:15 p. m. Dermatitis Venenata Due to Cosmetics and Industrial Irritants. Dr. John G. Downing. Discussion by Dr. Francis P. McCarthy.

March 29 — Hotel Kenmore. 8:15 p. m. Subject to be announced but to be related to diseases of the kidney. Dr. Albert A. Hornor.

May, 1938 — Annual meeting.

The censors meet on the first Thursdays of May and November in each year.

PLYMOUTH

Meetings will be held at 11 a. m. on November 18, January 20, March 17, April 21, May 19 and July 21.

SUFFOLK

January 19 — Joint meeting with Boston Medical Library.

March 15 — Joint meeting with Boston Obstetrical Society.

WORCESTER

At the following meetings, except the annual meeting, dinner will be at 6:15, to be followed by business session and scientific program.

December 8 — St. Vincent Hospital, Worcester.

January 12 — Worcester City Hospital, Worcester.

February 9 — Worcester State Hospital, Worcester.

March 9 — Memorial Hospital, Worcester.

April 13 — Hahnemann Hospital, Worcester.

May 11 — Afternoon and evening, annual meeting. Place and schedule of program to be announced.

BOOKS RECEIVED FOR REVIEW

Physical Therapy in Arthritis. Frank Hammond Krusen. 180 pp. New York: Paul B. Hoeber, Inc. $2.25.

The Rockefeller Foundation: International Health Division. Annual Report, 1936. 278 pp. New York: The Rockefeller Foundation, 1937.

The Diary of a Surgeon in the Year 1751-1752. John Knyveton. Edited and transcribed by Ernest Gray. 322 pp. New York and London: D. Appleton-Century Company, 1937. $2.50.

Crippled Children: Their treatment and orthopedic nursing. Earl D. McBride, in collaboration with Winifred R. Sink. Second edition. 379 pp. St. Louis: The C. V. Mosby Company, 1937. $3.50.

Methods of Treatment. Logan Clendening. Sixth edition. 879 pp. St. Louis: The C. V. Mosby Company, 1937. $10.00.

The Management of Fractures, Dislocations, and Sprains. John Albert Key and H. Earle Conwell. Second edition. 1246 pp. St. Louis: The C. V. Mosby Company, 1937. $12.50.

Eyestrain and Convergence. N. A. Stutterheim. 89 pp. London: H. K. Lewis & Company, Ltd., 1937. 7s. 6d.

A Diabetic Manual for the Mutual Use of Doctor and Patient. Elliott P. Joslin. Sixth edition, thoroughly revised. 219 pp. Philadelphia: Lea & Febiger, 1937. $2.00.

A Practical Treatise on Diseases of the Skin: For the use of students and practitioners. Oliver S. Ormsby. Fifth edition, thoroughly revised. 1334 pp. Philadelphia: Lea & Febiger, 1937. $12.00.

Orthodiascopy: An analysis of over seventeen hundred orthodiascopic examinations. Chester M. Kurtz. 247 pp. New York: The Macmillan Company, 1937. $3.50.

Arteriovenous Aneurysm: Abnormal communications between the arterial and venous circulations. Emile Holman. 244 pp. New York: The Macmillan Company, 1937. $5.00.

BOOK REVIEWS

Neurology. Roy R. Grinker. Second edition. 999 pp. Springfield and Baltimore: Charles C Thomas, 1937. $8.50.

The author, formerly with the University of Chicago and now head of the department of neuropsychiatry of the Michael Reese Hospital, published the first edition of his textbook in 1934. It had a wide sale, especially in medical schools, for the volume filled a need as a bridge between neuroanatomy and neurophysiology and the clinical aspects of neurology. Much emphasis was placed on neurophysiology, and the book reflects the great growth of this subject which had resulted from the impetus given it by Sherrington. The older textbooks, either written before the days of neurophysiologic advance or failing to keep up with it, offered little as compared with the great wealth of material set forth by Grinker. In the second edition the author has attempted to keep abreast of the physiologic field, and new material has been added on the brain cortex and the vegetative nervous system. The task, however, is almost beyond any individual, even as sound a student as Grinker. New and important advances appear in the technical journals almost every month, reflecting the rapidly changing status of our knowledge of neurophysiology. Grinker gives a fair summary, the best that can be found in any text.

In reviewing the previous edition of 1934, the weakness of the clinical side was pointed out. Little has been done to strengthen this part of the book in the new edition. In one subject, for instance, no paper since 1929 is cited, although much has been added since that date. The neurologist must not expect to find here much to help him in the clinic, except the strong physiologic background which, of course, he should have. For the internist, the older clinical books, such as those of Oppenheim or Gowers, or the more recent book by Brain, offer him the quickest approach to his clinical problems. This book, therefore, is a sound, useful text, within its limitations. The psychoses and the neuroses are not included. The new edition is only slightly larger than the old; a change in paper has made the illustrations clearer. Minor errors have been corrected and the chapter bibliographies revised and partly brought up to date.

Emanotherapy. F. Howard Humphris and Leonard Williams. 188 pp. Baltimore: William Wood & Company, 1937. $3.00.

This little volume is unique in that it sets forth many applications of radium emanation which are little known in this country and infrequently, if ever, used. Approximately the first half of the book is devoted to general and technical consideration of radon or radium emanation. The last six of the eleven chapters deal with the application of small amounts of radon to "goutiness and rheumatics," gynecology, dermatology, otorhinology, and a variety of other conditions. The book makes interesting reading, but the therapeutic value of this method of radon application might be questioned by many.

The Tercentenary of Harvard College. A Chronicle of the Tercentenary Year 1935-1936. 492 pp. Cambridge: Harvard University Press. 1937. $4.00.

This volume is a chronicle of the Tercentenary Year celebrated by Harvard University in 1935-1936. To these exercises came over eleven thousand alumni and seventy-one invited scholars of recognized eminence from all quarters of the globe. Five hundred and forty-six representatives from four hundred and ninety-eight universities situated in every state in the union and in forty-one foreign lands honored the University by their presence. America had never before seen such an academic pageant.

"One of the prime objects of the celebration, and in fact, its distinguishing characteristic, was . . . to demonstrate the functions and resources of a university." That this object was well fulfilled is amply attested to in this present volume, which may serve to remind those of us who attended of the events that transpired and which will surely be of interest and value to those of us who were unable to be present.

The first chapters are devoted to the organization of the celebration, and give in detail the activities in which the visitor to Harvard at that time might participate and the points of interest that he might visit. Special exhibits in the various departments of the university were designed to demonstrate the "functions and the resources of a university." One has but to read these chapters — and they are easily read — to realize with what meticulous care these preparations were made. One had but to attend the celebration to appreciate with what smoothness and precision the plans were followed out.

The exercises opened on November 7, 1935 — the beginning of the three hundredth year of Harvard College and the anniversary of John Harvard's birthday. Professor Morrison spoke of "Harvard's Past" — of the beginnings and of the history of that "schoale or colledge" founded November 7, 1636. We are reminded of the early hardships of this "colledge" where were erected "palings to protect from prowling wolves and Indians," and Professor Morrison goes on to point out that "the president had to take most of his salaries in commodities, including 'a goate of the Watertown rate,' which died." But, in spite of hard times, the college prospered and gradually the curriculum, at first rather austerely religious and philosophic, was improved and changed to be in tune with the times. The study of modern languages was introduced in 1820, that of modern history in 1870. It is perhaps worth while parenthetically to remark that the first course in pathologic anatomy to be offered in this country was in the Harvard Medical School in 1842.

There follows President Conant's address in which the unique privileges, advantages and obligations of a private university are clearly defined. The dangers inherent in too much governmental control are discreetly pointed out. "On the whole, the privately endowed universities are less likely to be influenced by utilitarian considerations than are the publicly supported institutions. . . . Independence and freedom from political control are the most valuable assets of our privately supported colleges and universities." One senses, perhaps, the realization on the part of those in authority that federal or state control might be more of a hindrance than advantage.

Brief accounts are given of the symposia offered by the various units of the university — the Medical School, Dental School, the School of Public Health and other departments.

There is an account of the opening of the package of letters sealed on September 8, 1836, by President Quincy and the sealing of a similar package to be opened by the president in 2036.

The exercises of the fall of 1936 are given in detail and here we may find Professor Rand's Latin salutatory oration, John Masefield's "Lines Suggested by the Tercentenary of Harvard College," the citations of the sixty-two honorary degrees, the address of President Angell, that "simple Vermont Yankee" who appeared "in partibus infidelium," and finally the congratulatory messages from the universities and learned societies in many parts of the world — two hundred in all. These messages, many in English, many in Latin, and some in foreign languages of the day, are most interesting. In general their tenor may be taken from the closing lines from the University of Cambridge — "Nil ergo amplius possumus vobis precari quam ut Fortuna quae tria iam saecula vobis faverit, semper arrideat" ("May the future smile upon you as has the past").

There is an appendix giving a detailed list of the papers presented before the various symposia.

Thus "out of smalle beginnings greater things have been produced by His hand that made all things of nothing and gives being to all things that are; and as one small candle may light a thousand, so the light here kindled hath shone to many, yea, in some sorte, to our whole nation."

This brief volume, illustrated to good effect by photographs of the major events, should be in the hands of each and every alumnus of Harvard University. Herein it is easy to read of the glories and hardships of both the past and the present of the "colledge" established "in silvestribus et incultis locis," anno Domini 1636.

Practical Talks on Kidney Disease. Edward Weiss. 176 pp. Springfield and Baltimore: Charles C Thomas, 1937. $3.00.

This small volume may be welcomed as an admirable interpretive statement of our present knowledge of diseases of the kidney. Beginning with the original description of Bright, it traces the changes in point of view which followed until the conceptions of the present day, including classification and terminology, have been reached. It may be recommended to all who have been confused by the conflicting teachings of the past. Still, after reading it one cannot avoid the reflection that kidney diseases are still an unsatisfactory subject in medicine. Advances in our understanding of them have, it is true, shown us the fallacy of certain therapeutic measures formerly in vogue and the advantage of certain more rational measures, but the prospect of their effectual control still seems remote.

Clinical Allergy. Louis Tuft. 711 pp. Philadelphia and London: W. B. Saunders Company, 1937. $8.00.

This is a good book. Among its merits lies the fact that it is published primarily for the general practitioner rather than for the expert allergist. It is well written in a straightforward, readable style, with primary emphasis on the practical instead of the theoretical aspects of the subject.

Divided into four sections, the author takes up, in turn, fundamental principles, basic etiologic types and characteristic clinical manifestations of allergy. He saves the final section for consideration of allergic dermatoses and of the interrelation of allergy and the other specialties.

This volume should fulfill the hopes of its writer and be of value to the general practitioner, medical student and beginner in the field of allergy.